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LIVER DOSAGE IN PERNICIOUS ANEMIA*

Failure of Quantitative Storage of Hematopoietic Principle

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CLEVELAND

TREATMENT of patients with pernicious anemia by parenteral liver extract has become such a well-established procedure that it needs no further discussion. The usual method involves the administration of conveniently sized doses of liver extract at regular intervals of one, two, three and, occasionally, four weeks. The size of each dose and the interval between treatments must be regulated by the requirements of the patient as determined by observation in each case.

Normal persons manufacture the hematopoietic principle effective in pernicious anemia by the interaction of intrinsic (gastric) factor and extrinsic (food) factor.[1] This reaction presumably takes place in the intestinal tract,[2] and the product of the interaction is recovered from the liver in the preparation of the liver extracts effective in the treatment of pernicious anemia. It has been thought that the liver might be a storehouse for the hematopoietic principle,[3–6] and that its only function is to release this principle as the necessity arises. If it were possible for the liver to store the hematopoietic principle quantitatively without any excretion or destruction, it is conceivable that large amounts of liver extract might be administered over a short period to patients with pernicious anemia and thus enable them to remain in remission as long as if the same total dose of liver extract were given in the usual manner of smaller doses at regular, frequent intervals. Miller,[7] in 1936, suggested this possibility and presented data showing that some such storage might take place. Strauss and Pohle[8] subsequently presented similar data indicating that, although some storage may take place, patients with pernicious anemia generally do not remain in remission so long when treated with single massive doses as when they receive the same total dose in smaller amounts at spaced intervals.

The observations reported here were made on 9 patients with pernicious anemia in remission and 13 patients with pernicious anemia in relapse. Six were men, and 16 were women. All had been observed at some previous time during both relapse and remission. The 9 patients in remission had been followed previously for ten to forty-six weeks during remission; during this time they received doses of liver extract at intervals of two or three weeks, and the individual requirement was ascertained. The 13 patients in relapse had also been followed from ten to forty-six weeks during a remission, so that their individual maintenance dosage of liver extract was similarly established. Subsequently, these 13 patients failed to keep scheduled appointments for treatment, so that when next seen they were in relapse, at which time the observations reported here were begun.

For purposes of discussion, patients were arbitrarily considered to be in remission when the red-cell count was 4,000,000 or more, with a hemoglobin of 90 per cent (14.0 gm. per 100 cc.). Values less than these constituted a relapse. All patients had typical Addisonian pernicious anemia, including the usual blood findings, absence of free hydrochloric acid after subcutaneous administration of histamine and varying degrees of posterolateral-column sclerosis. All had been seen in relapse at least once before the beginning of this study, and all had responded to liver extract or oral stomach preparations in the expected manner.

Figure 1 shows the results when the 9 patients

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in remission were treated with massive doses of liver extract. These patients received 55 to 140 *U.S.P.* units of parenteral liver extract[9] in ten to thirty days' time, after which no liver or liver extract was given until the blood showed evidence

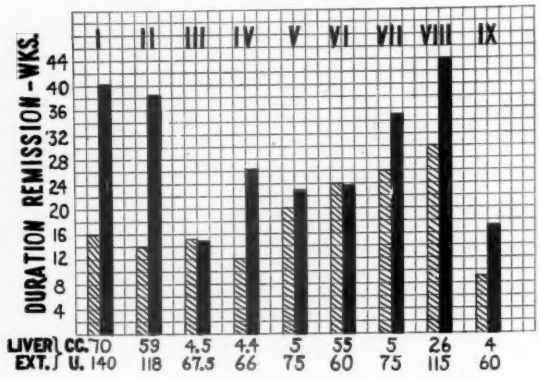

FIGURE 1. *Patients with Pernicious Anemia in Remission.*

The actual durations of remission (cross-hatched areas) following massive doses of liver extract are compared with the calculated durations of remission (solid areas) that would have obtained if the same amount of liver extract had been given in the usual intermittent doses.

of relapse as previously defined. In Figure 1, the cross-hatched bars represent the actual length of time the patients remained in remission following the massive liver treatment; the solid bars represent the calculated length of time the patients would have remained in remission had the same total dose of liver extract been administered in smaller amounts spaced at regular intervals of two or three weeks. In all but 3 of the 9 cases, relapses occurred much sooner with massive-dose therapy than they would have occurred with the intermittent-dose method. In Cases 3, 5 and 6, the interval of remission was about the same. The explanation of why these 3 cases were apparently able to store the liver extract quantitatively will be considered subsequently.

It must be mentioned, at this point, that there may have been some error in determining the actual maintenance dose of liver extract required by these patients when they were treated in remission with the usual small, intermittent doses. An effort was made to give the patients just enough liver extract to cause them to remain in remission. However, it is probable that a somewhat greater amount was given than was actually required, since none of the patients were allowed to relapse during the period of maintenance observation. Even though this factor caused the results of massive dose treatment to appear more favorable, they are generally not so good as those which would have been obtained had the same total dose of liver extract been given in small, regular, intermittent doses. Table 1 shows the volume and number of units of liver extract utilized per week in both the massive-dose and intermittent-dose methods of treatment.

It can also be seen from Table 1, by comparing doses in cubic centimeters with the units contained, that both crude and concentrated liver

TABLE 1. *Volume and Units of Liver Extract Utilized per Week by Patients with Pernicious Anemia in Remission, Using Massive-Dose and Intermittent-Dose Therapy.*

Case No.	Liver Extract Utilized per Week			
	Massive dose		Intermittent dose	
	cc.	*units*	*cc.*	*units*
1	4.37	8.74	1.74	3.48
2	4.21	8.42	1.53	3.06
3	0.30	4.50	2.30	4.60
4	0.37	5.50	2.50	2.50
5	0.25	3.75	0.18	3.26
6	2.08	2.08	2.10	2.10
7	0.84	3.71	1.31	2.62
8	0.44	6.66	1.74	3.48
9	0.19	2.88	2.10	2.10

extracts were employed in the study of these patients. We do not wish to discuss the relative merits of these two types at this time and only call attention to the fact that, so far as maintenance of blood levels is concerned, one type was as effective as the other.

The results when massive doses of liver extract were given to patients in relapse are shown in Table 2. In these cases, the duration of the actual

TABLE 2. *Attainment and Maintenance of Remission by Patients with Pernicious Anemia in Relapse After Treatment with Massive Doses of Liver Extract Given in Ten to Thirty Days.*

Case No.	Red-Cell Count*	Hemoglobin†	Liver Extract		Duration of Remission
	$\times 10^6$	%	*cc.*	*units*	*weeks*
10	1.30	38	130	260	17
11	1.70	50	165	330	17
12	2.10	62	80	160	19
13	0.60	24	70	140	15
14	1.50	53	190	380	26
15	3.20	87	115	230	22
16	3.50	92	85	185	13
17	3.60	76	80	160	13
18	3.80	65	50	100	17
19	3.30	70	60	120	16
20	2.60	60	45	90	29
21	1.20	32	120	240	16
22	3.90	80	70	140	13

*At beginning of treatment.
†100 per cent hemoglobin = 15.6 gm. per 100 cc.

remission cannot be compared with that which would have resulted if treatment had been instituted during remission, since there is no method of calculating how much liver extract these patients utilized before remission was attained. These 13 patients were given 90 to 380 units of liver ex-

tract intramuscularly in ten to thirty days. A maximal reticulocyte response and a rapid increase in red blood cells and hemoglobin occurred in each case. It is evident that these patients were able to attain and maintain remission for longer periods than if liver extract had been given in dosage sufficient only to produce a maximal reticulocyte response. All these patients attained remission blood levels and remained in remission for thirteen to twenty-nine weeks without further treatment of any sort.

As previously noted from Figure 1 and Table 2, there is considerable variation in a patient's ability to store liver extract. The most reasonable explanation of this depends on the fact that pernicious anemia is the result of a relative and not necessarily an absolute deficiency of gastric intrinsic factor. Goldhamer[10] has shown that patients with pernicious anemia have some intrinsic factor in their stomachs, although it is obviously not present in sufficient quantities to prevent the occurrence of anemia. If gastric juice is removed daily from certain of these patients, pooled until large quantities are obtained, and administered to the same or other patients with pernicious anemia in relapse, a hematopoietic response ensues, similar to that produced with normal gastric juice and indicating that some intrinsic factor is present.

It is reasonable to assume, therefore, that there are all degrees of pernicious anemia from mild to severe, depending on the degree of deficiency of intrinsic factor. The patients with mild cases, although they do not manufacture enough hematopoietic principle to prevent anemia, obviously manufacture more hematopoietic principle than those with severe cases and, hence, greater deficiencies, and the former need less liver extract than the latter.

To test this hypothesis, we selected 2 patients who had mild pernicious anemia as evidenced by the fact that they did not require so much liver or liver extract to maintain remission as the average case of pernicious anemia did. The first patient, H. P., had been kept in remission for several months by the daily feeding of whole liver. At the beginning of the observation period shown in Table 3, all liver and stomach products were removed from the diet, and 120 gm. of beef or two eggs daily were added — both beef and eggs are known to be good sources of extrinsic factor.[11] On this regimen, the patient remained in remission for a period of thirty-nine weeks, although no specific therapy was administered. At the end of this period, she was unwilling to follow the diet longer, and therapy with liver was resumed.

TABLE 3. *Data on Patient H. P.*

Duration of Treatment*	Red-Cell Count	Hemoglobin
weeks	$\times 10^6$	%
0	4.20	100
7	4.61	101
11	5.09	102
13	4.63	101
19	4.70	98
27	4.63	97
35	4.58	95
39	4.50	92

*The diet included 120 gm. of beef or two eggs daily. No liver or liver extract was administered during this period. Prior to this period the patient had maintained herself on whole liver by mouth.

The second patient, C. R., in addition to pernicious anemia, had hypertension and angina pectoris. Twenty-eight weeks preceding the observation period recorded in Table 4, the patient received a single dose of 10 units (2 cc.) of liver extract intramuscularly. At the beginning of the period recorded, 60 to 120 gm. of beef or one to two eggs daily were added to the diet. The patient disliked both these foods and had not been eating either regularly. She remained in remission for fifty weeks, at the end of which she refused to include the items in her diet, and the blood showed a relapse. At this time, she was given 45 gm. of brewer's yeast daily. This material, which has a high protein content, is also an excellent source of extrinsic factor.[12] The blood showed improvement, but after six more weeks the patient

TABLE 4. *Data on Patient C. R.*

Period of Observation	Therapy*	Red-Cell Count	Hemoglobin
weeks		$\times 10^6$	%
0	60 to 120 gm. beef or 1 to 2 eggs daily	3.80	94
2	60 to 120 gm. beef or 1 to 2 eggs daily	4.90	102
4	60 to 120 gm. beef or 1 to 2 eggs daily	4.89	101
6	60 to 120 gm. beef or 1 to 2 eggs daily	5.00	103
8	60 to 120 gm. beef or 1 to 2 eggs daily	4.66	100
11	60 to 120 gm. beef or 1 to 2 eggs daily	4.41	96
13	60 to 120 gm. beef or 1 to 2 eggs daily	4.70	101
15	60 to 120 gm. beef or 1 to 2 eggs daily	4.56	100
17	60 to 120 gm. beef or 1 to 2 eggs daily	4.60	99
19	60 to 120 gm. beef or 1 to 2 eggs daily	4.60	97
21	60 to 120 gm. beef or 1 to 2 eggs daily	4.55	99
23	60 to 120 gm. beef or 1 to 2 eggs daily	4.70	104
26	60 to 120 gm. beef or 1 to 2 eggs daily	4.71	99
29	60 to 120 gm. beef or 1 to 2 eggs daily	4.55	99
33	60 to 120 gm. beef or 1 to 2 eggs daily	4.81	101
37	60 to 120 gm. beef or 1 to 2 eggs daily	4.49	98
40	60 to 120 gm. beef or 1 to 2 eggs daily	4.63	98
44	60 to 120 gm. beef or 1 to 2 eggs daily	4.48	97
48	60 to 120 gm. beef or 1 to 2 eggs daily	4.56	97
50	60 to 120 gm. beef or 1 to 2 eggs daily	3.53	94
51	45 gm. yeast daily	4.01	
53	45 gm. yeast daily	4.02	89
55	45 gm. yeast daily	4.49	98
57	5 units liver extract intramuscularly	3.70	89
61	60 to 120 gm. beef or 1 to 2 eggs daily	4.71	93
65	60 to 120 gm. beef or 1 to 2 eggs daily	4.49	89
69	10 units Campolon	3.90	82
73		4.49	90
77		4.35	89
81		4.27	87
85	22 units liver extract intramuscularly	3.85	80
89	20 units liver extract intramuscularly	3.91	85
93		4.90	97
97		4.26	84
101		4.99	97
105		4.45	93

*Patient had received 10 units of liver extract intramuscularly twenty-eight weeks preceding the beginning of this period; no other antianemic substance given.

refused to ingest the yeast; another relapse occurred. She was given 5 units (1 cc.) of liver extract intramuscularly, with good results. At that time, she again started to eat beef or eggs, but because of her dislike for these foods, frequently omitted them from her diet. In spite of this, she received a total of only 52 units of liver extract intramuscularly during another forty-eight weeks. The patient decided that treatment should not be given so long as the red-cell count was over 4,000,000; this explains why the hemoglobin values were allowed to fall below 90 per cent (14.0 gm. per 100 cc.) on several occasions. When last seen, the patient felt perfectly well, showed no signs of progression of the posterolateral-column sclerosis, and had no complaints except frequent, mild attacks of angina pectoris.

There can be no doubt that these 2 patients represent true cases of pernicious anemia. Both were observed in severe relapse, and both reacted to liver with the usual reticulocyte response and increase in red-cell count and hemoglobin. Free gastric hydrochloric acid was absent in both after histamine was administered. The first patient had a moderate amount of posterolateral-column sclerosis. During subsequent periods of observation, it was found that even when these patients were given diets containing what is considered to be a normal amount of protein, an occasional dose of liver or liver extract was needed to maintain normal red-cell counts and hemoglobin levels. This is demonstrated in the last period of Table 4, but is not illustrated by the course of the first patient (Table 3), who has not been followed so regularly since the completion of the period shown.

It might reasonably be assumed that these two patients went into spontaneous remission coincident with the institution of the diet containing larger amounts of extrinsic factor, since it is well known that patients with pernicious anemia can undergo spontaneous remission lasting for months or even years. Although the explanation of such remissions has not been understood, it seems likely that either a spontaneous increase in gastric intrinsic factor or an increase of extrinsic factor in the diet might account for them. In the two cases described above, we believe that spontaneous remission occurred as a result of increasing extrinsic factor in the diet. It is probable that certain cases of spontaneous remission observed in the past resulted when patients, for one reason or another, increased the amount of extrinsic factor in the diet.

Discussion

It is unnecessary to assume any actual storage of hematopoietic principle to account for the fact that patients with pernicious anemia treated with massive doses of liver extract remain in remission for varying long periods. Regardless of the degree of deficiency of the gastric intrinsic factor, any patient can attain and maintain remission for some time after liver extract is given. The time that remission is maintained is longer in the patients with mild cases, who produce moderate amounts of hematopoietic principle, than it is in those with severe cases, who produce less hematopoietic principle.

The 2 cases maintained on extrinsic factor for long periods were sufficiently mild that only a small amount of extraneous hematopoietic principle was necessary to augment that made by the patients themselves. The fact that addition of extrinsic factor improves the formation of hematopoietic principle has been interpreted to be the result of a mass-action chemical phenomenon.[12] Since intrinsic factor added to extrinsic factor equals hematopoietic principle, increasing extrinsic factor causes an increase in the formation of hematopoietic principle, even though the intrinsic factor is present in less than normal amount.

Thus, the variation in amount of liver extract required by different patients is adequately explained. If the deficiency of intrinsic factor is relatively small and the amount of extrinsic factor in the diet is relatively large, less liver extract is necessary than if the reverse is true.

Summary and Conclusions

Patients with pernicious anemia in remission given large doses of liver extract within a brief period remain in remission for varying periods. This time is generally not so long as that when the same total dose of liver extract is administered in small, intermittent doses.

Patients with pernicious anemia in relapse given large doses of liver extract in a short period attain and maintain remission for varying lengths of time without further treatment.

If hematopoietic factor is stored in the body, such storage is not quantitative when large doses of liver extract are administered in a short period. The fate of the unused hematopoietic principle is unknown.

By augmenting the extrinsic factor in the diet, two patients with mild pernicious anemia were maintained in remission for long periods without any specific treatment.

The degree of deficiency of intrinsic factor and the amount of extrinsic factor in the diet of patients with pernicious anemia probably account for the individual variation in requirements of liver extract.

References

1. Castle, W. B. Observation on the etiologic relationship of achylia gastrica to pernicious anemia. I. The effect of the administration to patients with pernicious anemia of the contents of the normal human stomach recovered after ingestion of beef muscle. *Am. J. M. Sc.* 178:748-764, 1929.
2. Castle, W. B., Heath, C. W., Strauss, M. B., and Heinle, R. W. Observations on the etiologic relationship of achylia gastrica to pernicious anemia. VI. The site of the interaction of food (extrinsic) and gastric (intrinsic) factors: failure of *in vitro* incubation to produce a thermostable hematopoietic principle. *Am. J. M. Sc.* 194:618-625, 1937.
3. Wintrobe, M. M., and Shumacker, H. S. Occurrence of macrocytic anemia in association with disorder of the liver. *Bull. Johns Hopkins Hosp.* 52:387-407, 1933.
4. Van Duyn, J. Macrocytic anemia in disease of the liver. *Arch. Int. Med.* 52:839-851, 1933.
5. Schiff, L., Rich, M. L., and Simon, S. D. The "hematopoietic principle" in the diseased human liver. *Am. J. M. Sc.* 196:313-321, 1938.
6. Wilkinson, J. F., and Klein, L. The hematopoietic activity of the normal and abnormal human liver, with special reference to pernicious anemia. *Quart. J. Med.* 3:341-359, 1934.
7. Miller, F. R. Effect on pernicious anemia of massive doses of parenteral liver extract. *Proc. Soc. Exper. Biol. & Med.* 33:580-582, 1936.
8. Strauss, M. B., and Pohle, F. J. The duration of remission in pernicious anemia with liver therapy. *J. A. M. A.* 114:1318-1370, 1940.
9. Report on potency of liver products. *J. A. M. A.* 110:812, 1938.
10. Goldhamer, S. M. The gastric juice in patients with pernicious anemia in induced remission. *Am. J. M. Sc.* 193:23-28, 1937.
11. Castle, W. B., and Minot, G. R. Pathological physiology and clinical description of the anemias. In *Oxford Medicine.* Vol. II, Chap. 16. New York: Oxford University Press, 1936. P. 651.
12. Heinle, R. W., and Miller, F. R. Yeast as an extrinsic factor in relation to pernicious anemia. *J. Clin. Investigation* 18:257-259, 1939.

CONTROLLED ADMINISTRATION OF FLUID IN SURGERY*

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ROBERT Boyle,[1] the physicist, was interested in the density of many things. In 1683, while weighing blood and serum, he noted that in acute disease the specific gravity was higher and in chronic disease lower than normal. In the next century, Jurin[2] confirmed these observations. However, it was not until the nineteenth century that this knowledge was applied clinically. O'Shaughnessy[3] in England and Wittstock[4] in Germany demonstrated in 1831 that in Asiatic cholera the specific gravity of blood is considerably higher than normal.

Roy,[5] using a simplified method of obtaining the density of blood, showed by animal experimentation in 1884 that the blood becomes heavier in shock. This phenomenon occurs before any fall in blood pressure. Roy wished to find where the fluid lost from the blood could be found. By carrying out density determinations on the intestinal wall and on other organs, he showed that, in shock, fluid shifts from the blood into these tissues.

The first practical application of Roy's work was in India. Rogers,[6] the Surgeon General of India, considered the mortality in Asiatic cholera to be too high. In this disease, the patient goes into typical dehydration collapse due to vomiting, sweating and copious rice-water stools. A cold clammy skin, weak thready pulse, great muscular weakness and marked prostration supervene. The only pulsating vessels are often the carotid arteries. The blood is viscid and thick, and the specific-gravity values of peripheral blood are often above 1.070. Besides hemoconcentration, there is a decrease in the sodium, an increase in the potassium concentration of the blood and a fall in the blood chloride and bicarbonate contents.

Both hypotonic and isotonic solutions had given disappointing results in cholera. Rogers introduced a slightly hypertonic (1.5 per cent) sodium chloride solution, and controlled the large administration of fluid by following the specific gravity of the peripheral blood. At times, as much as 10 to 12 liters was given within twenty-four hours before hemodilution was secured. Rogers issued an order that fluids should be stopped when the specific gravity of the blood reached 1.050. This was to prevent giving too much. This type of therapy reduced the mortality rate from Asiatic cholera at the Calcutta General Hospital from 59 per cent during the decade 1895–1905 to 26 per cent during the years 1910–1914.

The similarity between Asiatic cholera, intestinal obstruction and traumatic shock has often been noted. The chemical changes in the blood are identical.[7]

During World War I, Cannon[8] reported hemoconcentration in soldiers suffering from wound shock. Erythrocyte counts of 6,000,000 to 8,000,000 were associated with high mortality, especially if there was a great disproportion between the counts taken on capillary and those taken on venous blood. For some reason, this very im-

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portant observation is not widely known. Today, specific-gravity determinations are supplanting erythrocyte counts because of their far greater accuracy and sensitivity.[9-11]

The second test that is of value in assaying the degree of dehydration is the hematocrit or cell volume. During the early part of the nineteenth century, it was appreciated that in cholera the blood lost water. O'Shaughnessy[3] applied the term "crassamentum" to the solid matter that settled out on standing. In some cholera cases, the water loss from the blood was so extreme as to leave only 27.5 per cent fluid and 72.5 per cent solids. This may be taken as the first objective measurement of decreased plasma volume in shock.

Blix[12] presented at Upsala the first *Haematokrit*. It was modeled after the *Laktokrit* used in the dairy industry. With this apparatus, Hedin[13] in 1891 reported values for normal men and women. In dehydration, whatever the cause, an increase in the hematocrit is characteristic.

The third test weighs a drop of plasma. This gives the total plasma solids and serves as another measure of dehydration.

The importance of the plasma proteins is now well recognized. One of their functions is protective. They also serve as a measure of dehydration. On account of the work of Weech and his associates,[14] one is able to compute the total plasma proteins from the specific gravity of the plasma. This is readily accomplished by using the modified Barbour and Hamilton apparatus[7] for the measurement of the specific gravities of body fluids.

These four values — the specific gravity of the peripheral blood, the hematocrit, the specific gravity of the plasma and the total protein content — can be determined within fifteen minutes, and afford accurate information about the state of the peripheral and venous circulating systems. They furnish data concerning the state of hydration. In cases of injury, changes of the specific gravity of capillary blood herald the approach of shock. One is thus forewarned and can institute therapy at a time when such corrective measures are most effective. These tests can differentiate shock due to internal blood loss from typical dehydration or traumatic shock before changes in blood pressure and before the appearance of the classic symptoms of shock.

TABLE 1. *Blood Findings in a Patient with Multiple Injuries, including a Compound Fracture of the Tibia.*

DATE	TIME	HEMATOCRIT	WHOLE BLOOD SPECIFIC GRAVITY	PLASMA SPECIFIC GRAVITY	PLASMA PROTEINS	PLASMA POTASSIUM	PLASMA SODIUM	PLASMA CHLORIDE	FLUID THERAPY
		%			*gm./ 100 cc.*	*milliequiv./ liter*	*milliequiv./ liter*	*milliequiv./ liter*	
April 5	8:30 p.m. (admission)	44.9	1.0561	1.0293	7.62	3.6	141.6	105.8	Dried serum equal to 1500 cc., intravenously; 300 cc., by mouth.
	10:30 p.m.		1.0503						
	12:00 midnight (end of operation)	30.6	1.0484	1.0255	6.33	4.1	142.2	105.0	
April 6	10:30 a.m.	35.3		1.0261	6.53	5.3	137.6	104.8	2700 cc., by mouth; 1000 cc., subcutaneously; 500 cc., transfusion
April 7									2950 cc., by mouth
April 8	9:00 a.m.	26.3		1.0256	6.36	3.6	131.2	100.0	2650 cc., by mouth
April 9									3200 cc., by mouth; 500 cc., transfusion.
April 10	9:20 a.m.	29.1		1.0257	6.39				

In the postoperative care of the patient, the data furnished by these tests indicate whether blood should be administered; whether plasma and proteins should be used; whether salt solution is indicated; and, above all, when fluid therapy should be stopped. In addition to these helpful points, one can ascertain whether the fluid given is being utilized. In treating impending shock, should the blood become more concentrated after the administration of saline, one is immediately warned of the approach of a grave crisis. It is in just this state that the use of a potent adrenocortical hormone, along with salt, causes a reduction of hemoconcentration and a decrease in blood viscosity.

The restoration of blood volume in shock is essential. The restoration of blood volume with the proper type of fluid is even more important. In cases with renal failure or anuria, the flooding of the vascular system with intracellular water is poor therapy. For normal function, the differential salt concentration between the intracellular and extracellular compartments is necessary. Factors that upset this balance are harmful, in particular hypertonic solutions given in the dehydrated

state. Kidney function must be restored early in injury. The accumulation of intracellular salts in the blood plasma, due both to damage and to failure of excretion, tends to change the normal state and was equivalent to 1500 cc. of liquid) was started intravenously, and the patient taken to the operating room for débridement and fixation of the fracture.

The cell volume and specific gravity of the peripheral blood were within normal limits (Table 1 and Fig. 1).

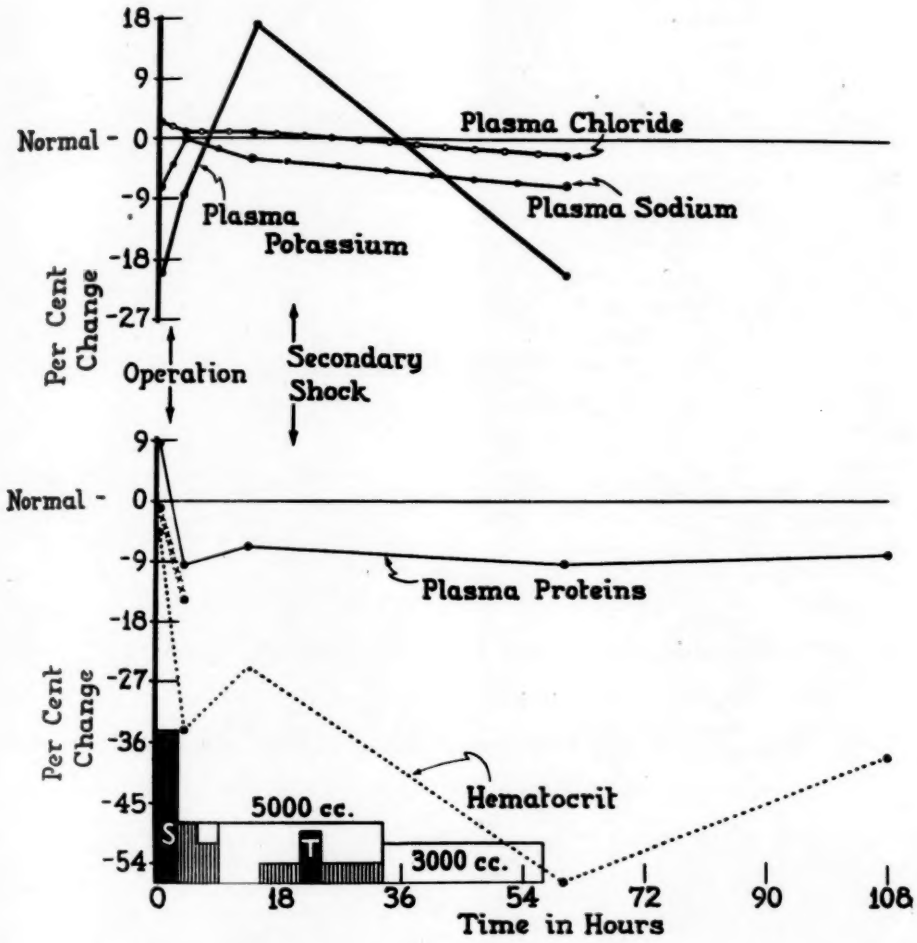

FIGURE 1. *Traumatic Shock Due to an Automobile Accident: Multiple injuries, with compound fracture of the tibia.*

ratio between intracellular potassium and extracellular sodium ions.

The following case of traumatic shock illustrates some of these points.

CASE REPORT

S. G. (P. H. 638287), a 59-year-old man, was brought to the hospital by ambulance a few minutes after an automobile accident in which he had sustained multiple contusions, lacerations and a compound fracture of the tibia. The patient was in primary shock, with a blood pressure of 80/60 and a pulse of 60. The leg had been fixed in a Thomas splint. The patient was conscious and oriented, but could not recall details of the accident.

He was given ¼ gr. of morphine after blood had been secured for chemical studies and grouping. An infusion of serum (which had been reconstituted from the dried

The specific gravity of the plasma and the plasma proteins were elevated, findings that suggested a case of secondary anemia exhibiting hemoconcentration. The values of the sodium, potassium and chloride concentrations were not available at this time and illustrate that these determinations are valueless in directing emergency therapy on account of their time-consuming nature. They afford, however, valuable information about the effects of therapy when one reconsiders a case.

Blood dilution was secured with the serum, as shown by the falls in the hematocrit, specific gravity of capillary blood and plasma proteins. Eventually, there were decreases in the chloride and sodium concentrations, but the greatest change was a marked increase in the potassium concentration (from 3.6 to 5.3 milliequiv. per liter)[15] within 18 hours after the accident. Physiologic saline and Eschatin (adrenocortical extract) were withheld in the initial treatment because we wished to ascertain the effect

of serum alone on both the clinical and chemical aspects of shock.

On the following day, the patient went into typical secondary shock, which was combated with oxygen, infusions of physiologic saline and blood transfusion.

Comment. The administration of adrenocortical extract and salt during the initial treatment might have prevented the changes in sodium, potassium and chloride concentrations. The 58 per cent decrease in cell volume may have indicated overdilution of the blood, and points to the recommendation of giving 500 cc. of blood with every 500 cc. of plasma or serum, as recently advocated by Kekwick and his co-workers.[16]

Summary and Conclusions

Four simple tests based on elementary physical chemistry are presented as a means of judging the state of hydration in the capillary and venous circulating systems. Their value lies in their simplicity, reproducibility and ease of mastery. Their practicability lies in the minimum amount of equipment necessary.

These tests are useful in shock, since they forewarn of its approach and hence allow early therapy. One case of shock is presented in which 1500 cc. of serum was used. The overdilution of the blood and the change in the electrolyte pattern indicate that blood should have been given along with the serum and suggest that the administration of sodium and adrenocortical extract might have lessened the electrolyte changes.

References

1. Boyle, R. *Memoirs for the Natural History of Humane Blood, Especially the Spirit of That Liquor.* 289 pp. London: S. Smith, 1683.
2. Jurin, J. Experiments relating to the specific gravity of human blood. *Philosophical Tr. Roy. Soc. London* 5:326-333, 1719.
3. O'Shaughnessy, W. B. Chemical pathology of cholera. *Lancet* 2:225-232, 1832.
4. Wittstock, C. Chemical researches into the nature of cholera. *Lancet* 1:169-171, 1833.
5. Roy, C. S. Note on a method of measuring specific gravity of the blood for clinical use. *J. Physiol.* 5:ix-xi, 1884.
6. Rogers, L. *Cholera and Its Treatment.* 236 pp. London: Oxford University Press, 1911.
7. Scudder, J. *Shock: Blood studies as a guide to therapy.* 315 pp. Philadelphia: J. B. Lippincott Co., 1940.
8. Cannon, W. B. *Traumatic Shock.* 201 pp. New York: D. Appleton Co., 1923.
9. Barbour, H. G., and Hamilton, W. F. Blood specific gravity: its significance and a new method for its determination. *Am. J. Physiol.* 69:654-661, 1924.
10. *Idem:* The falling drop method for determining specific gravity. *J. Biol. Chem.* 69:625-640, 1926.
11. *Idem:* The falling drop method for determining specific gravity: some clinical applications. *J. A. M. A.* 88:91-94, 1927.
12. Blix: cited by Hedin.[13]
13. Hedin, S. G. Der Hämatokrit, ein neuer Apparat zur Untersuchung des Blutes. *Skandinav. Arch. f. Physiol.* 2:134-140, 1891.
14. Weech, A. A., Reeves, E. B., and Goettsch, E. The relationship between specific gravity and protein content in plasma, serum, and transudate from dogs. *J. Biol. Chem.* 113:167-174, 1936.
15. Zwemer, R. L., and Scudder, J. Blood potassium during experimental shock. *Surgery* 4:510-527, 1938.
16. Kekwick, A., Marriott, H. L., Maycock, W. d'A., and Whitby, L. E. H. Diagnosis and treatment of secondary shock; a study of twenty-four cases. *Lancet* 1:99-103, 1941.

PRIMARY CARCINOMA OF THE URETHRA IN THE MALE*

Report of a Case

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PRIMARY carcinoma of the urethra in the male is a comparatively rare disease. The first authentic case was reported in 1861 by Hutchinson.[1] In October, 1939, Kreutzmann and Coloff[2] searched the entire medical literature, and abstracted almost all the original case reports. With the addition of their own 2 cases, they brought the total of reported cases to 150. We report the following case because it serves well to illustrate the usual clinical course that this disease follows, the etiologic factors most commonly implicated and the diagnostic pitfalls most frequently encountered.

Case Report

A. L., a 58-year-old man, was admitted to the Lincoln Hospital on December 31, 1938. The patient had had some preliminary examination and treatment in another institution for the 2½ months directly preceding admission. Thirty-five years before hospitalization, he had had gonorrheal urethritis. He had no symptoms referable to the genitourinary tract until 5 years prior to entry, when he developed difficulty in starting the urinary stream, some dribbling and occasionally a drop or two of bleeding at the end of micturition. This, associated with severe burning and urgency, made him seek treatment. He was seen at two hospital outpatient clinics, and was told that he had a urethral stricture. He was treated by numerous and repeated dilatations, and appeared to be peculiarly unresponsive to therapy. Each treatment was followed by severe pain and bleeding. The stricture did not seem dilatable. The patient was admitted to the wards of one of these first hospitals because of the fact that he had developed a markedly stammering urinary stream, frequency, nocturia and a urethral discharge. He had 200 cc. of turbid residual urine. X-ray studies of the kidneys, ureter and bladder showed no abnormalities. Cystoscopic examination revealed what appeared to be numerous strictures along the posterior urethra, moderate prostatic enlargement and generalized cystitis. It was believed that the patient's symptoms were largely due to the prostatic hypertrophy, and that they could be alleviated by prostatectomy. Hence, a bilateral vasectomy and suprapubic cystotomy were performed, in preparation for enucleation of the prostate. Ten days later, there was a profuse urethral discharge and marked perineal induration. With the appearance of a fluctuant mass, an incision was made in the perineum, and 200 cc. of foul pus was obtained. The perineal induration increased and spread, requiring repeated incisions and drainage. About a week before the patient entered Lincoln Hospital, it

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was found that sounds could not be passed into the bladder because of obstruction at the junction of the membranous and prostatic portions of the urethra. Nor could sounds be passed into the bladder through the perineal incisions. Fluid injected into the urethral meatus came through the perineal wounds.

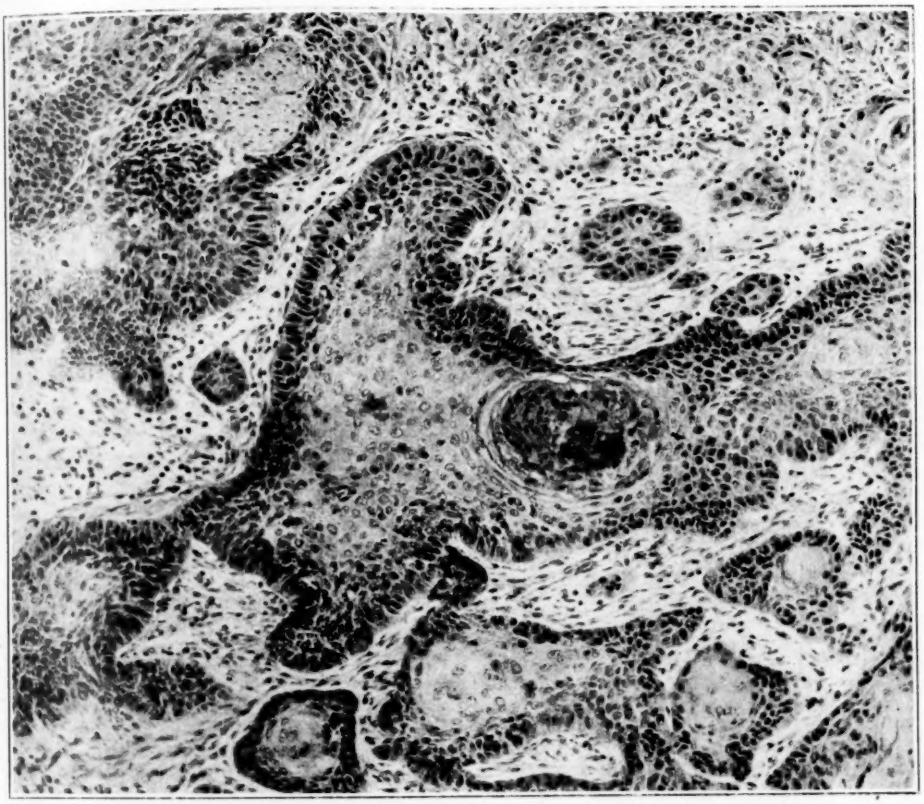

FIGURE 1. *Typical Acanthoma, Showing Numerous Keratinizing Pearls.*

On admission to Lincoln Hospital, the patient appeared acutely ill and cachectic. On January 26, 1939, after he had shown some improvement in his general condition, the perineum was completely exposed by enlarging the previous incisions. All necrotic tissue was removed, and the wound was irrigated and thoroughly packed. With increased drainage, the patient improved somewhat, but on February 14, because of extension of the infection in the perineum, the area was again incised. Suppuration involving the left ischiorectal fossa as high up as the left femoral triangle was found. There was marked sloughing of the bulbous and membranous urethra, with a urethroperineal fistula. The entire perineal area contained what seemed to be dense, cauliflowerlike inflammatory masses. Because of this appearance and the indolent healing, cancer was suspected, and a specimen removed for biopsy. Histologic examination of this tissue revealed that the mass was a typical squamous-cell epithelioma of the adult type (Fig. 1), the commonest type of cancer of the urethra. X-ray examination of the pelvis, lumbar spine and long bones showed no evidence of metastases. There was no adenopathy.

The patient failed rapidly and expired about 1 month after this operation. Autopsy revealed that the membranous and bulbous portions of the urethra were entirely destroyed by a cauliflowerlike tumor (Fig. 2), which extended throughout the entire length of these parts of the urethra.

Carcinoma of the urethra is a slowly progressive disease, affecting most frequently the membranous and bulbous portions of the urethra. Its recognition and course depend to some degree on the depth of the lesion in the urethra.

The initial symptoms of the disease are similar to and almost always mistaken for those of urethral stricture. However, suspicion should be aroused if presumable urethral strictures appear unresponsive to the usual treatment, or if perineal abscesses are intractable. Spread is by direct extension, with involvement of wide areas, which ultimately become necrotic and infected. Metastases are unusual, and regional adenopathy is most frequently due to infection. Distant metastasis is almost never seen, but when it does occur, the lung is the most frequent site.

The symptomatic course is divided into four stages by Kretchmer,[3] as follows: dysuria, retention and urethral discharge — the latter, if hemorrhagic, should lead one to suspect cancer; local tumor formation; periurethral infiltration with urine; and sinus formation. It is not until the latter two stages that carcinoma is suspected, so that diagnosis is generally late.

The etiology of urethral carcinoma, like that of all neoplastic disease, remains unknown. The

commonly held belief is that the condition is a metaplasia resulting from inflammatory irritation — in a large percentage of cases, gonorrheal urethritis is a common predecessor — or from repeated trauma, such as that of repeated dilatations.

Prognosis, which as a rule is very poor, can be improved only by early treatment. This necessitates early diagnosis. More frequent urethroscopies, with biopsy, in cases of intractable stricture, periurethral abscesses and sinuses that fail to heal, would increase the number of cases recognized.

Treatment consists in either radical resection or deep x-ray therapy, or both.

Summary

A case of urethral carcinoma in the male is presented. The usual clinical course, the diagnostic pitfalls and the etiologic theories are illustrated and discussed. A plea is made for careful study, with biopsy, of intractable strictures, periurethral abscesses and sinuses that fail to heal, to facilitate early diagnosis and to improve the prognosis.

FIGURE 2. *Gross Specimen Removed at Autopsy.*

A — bladder; B — *prostate;* C — *tumor mass, infiltrating and destroying the bulbous and membranous urethra;* D — *point of origin of tumor (about 2 cm. proximal to the glans).*

References

1. Hutchinson: cited by Wishard, W. N., Jr., and Bodner, H. Primary carcinoma of male urethra. *J. Urol.* 42:35-46, 1939.
2. Kreutzmann, H. A. R., and Coloff, B. Primary carcinoma of the male urethra. *Arch. Surg.* 39:513-529, 1939.
3. Kretchmer: cited by Wishard and Bodner.[1]

MENINGOCOCCEMIA WITHOUT MENINGITIS*

Report of a Case

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MENINGOCOCCEMIA, as a disease entity, without meningitis or other complications, has been known only in the last forty years, the first case having been described by Salomon[1] in 1902. Since then, the disease has been widely reported.

Carbonell and Campbell[2] have defined and described the disease clearly and completely in their report of 3 cases, which, however, were treated with serum just at the dawn of sulfanilamide chemotherapy. Since sulfanilamide and its derivatives have been available, about a dozen cases thus treated have been reported, without a fatality; all were marked by prompt and complete recovery.

In 1937, Schwentker, Gelman and Long[3] reported briefly a case of uncomplicated meningococcemia in a series of meningococcic infections, which was successfully treated with sulfanilamide. Zendel and Greenberg[4] reported an uncomplicated case in which the patient, ill three weeks when treatment was begun, recovered rapidly. Dimson,[5] in 1938, used pyridine (M. & B. 693), with recovery in six days after the beginning of treatment. Craven,[6] in 1938, reported rapid clearing of all symptoms with complete recovery in a man ill with uncomplicated meningococcemia for seven weeks before treatment was begun. Long and Bliss[7] briefly mention "five cases suffering from acute meningococcemia without signs of meningitis in whom intensive therapy with the drug gave excellent curative results." Binns and Clancy,[8] in 1939, reported 2 additional cases much like the others: a child of twelve years ill for two months, and a forty-five-year-old man ill for seven weeks, before accurate diagnosis was made. Both patients rapidly recovered after sulfanilamide therapy was begun. Levy,[9] in 1937, treated a two-year-old girl with both subcutaneous and oral therapy for nine days, with spectacular results. Kattwinkel[10] recently reported a case in which, with justification, the diagnosis of gonococcemia was originally made; the patient, a twenty-two-year-old woman, recovered rapidly following adequate oral doses of sulfanilamide. An additional case is reported below.

CASE REPORT

A 55-year-old woman was admitted to the hospital on February 29, 1940, complaining of chills and fever, maculopapular lesions on the face, trunk and extremities, and joint pains.

On February 15, 1940, the patient went to bed feeling quite well. She was awakened during the night with a marked chill. She took some aspirin and went back to sleep. The next morning, she felt fairly well, except for a mild sore throat and a stuffy feeling in her nose. At noon, she was nauseated, and vomited, with relief. The next day, February 17, however, she had another chill and developed high fever, and pain developed in many joints. She was given large doses of salicylates and bicarbonate of soda. The following day, a maculopapular rash was noted on both legs below the knees. Every 2nd or 3rd day from that time on, she developed a severe chill followed by high fever, varying between 103 and 105.4°F., each fastigium being followed by a fresh crop of maculopapular lesions, which gradually appeared over the entire body, accompanied by exacerbations of the polyarthralgia. No heat, redness or swelling appeared in any joints. During the remissions of fever, the patient became surprisingly well. Urinalysis was normal; the white-cell count was 12,800, with 82 per cent polymorphonuclears. A blood smear was negative for malaria. On February 29, 2 weeks after the onset, she agreed to hospitalization. The past history was negative for rheumatic heart disease, and was otherwise not pertinent.

On admission, the temperature was 99.2°F., the pulse rate 110, the respiratory rate 20, and the blood pressure 102/60. Physical examination revealed a fairly well-nourished and well-developed middle-aged woman in no acute distress. The skin showed many reddish-pink macules and papules over the entire body, predominately on the legs, some of which faded on pressure. One lesion on the left ankle was crusted. The lesions varied in size from several millimeters to 1 cm. in diameter. The older lesions were brownish. The eyes reacted normally to light and accommodation. The fundi were normal. There was no stiffness of the neck. The lungs were clear. The heart rate was rapid, but there were no murmurs, thrills or enlargement. The abdomen was normal, except for skin lesions and an old surgical scar. There was slight inguinal adenopathy. Neurologic examination was entirely negative, including tests of the cranial nerves and the sensory and motor systems. All reflexes were active, and the Kernig, Brudzinski and Babinski signs were negative.

The red-cell count was 3,800,000 with a hemoglobin of 72 per cent, and the white-cell count 12,900 with 85 per cent polymorphonuclears. There were slight poikilocytosis, anisochromia, polychromia, no erythroblasts and normal platelets. The clotting time was 1 minute, and the bleeding time 2 minutes and 15 seconds. The sedimentation rate (corrected) was 0.7 mm. per min. The blood Hinton reaction was negative; the nonprotein nitrogen of the blood serum was 27 mg. and the blood sugar 71 mg. per 100 cc. Urinalysis showed the slightest possible trace of albumin and no sugar, with rare red and white blood cells in the sediment.

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Rheumatic fever, arthritic purpura, spotted fever, typhoid and undulant fever were considered, and blood was submitted to the laboratory. The patient meanwhile was given 60 to 90 gr. of salicylates daily, which controlled the joint pains quite well. These pains gradually subsided during the 1st week of hospital stay. On March 2, 4 and 6, the patient had further severe chills and high fever, new skin lesions following each attack.

Nose and throat cultures taken on March 7 were positive for *Micrococcus catarrhalis* on March 12. On March 7, the laboratory reported that the blood culture on February 29 showed meningococci, identified by sugar fermentations. The diagnosis was also checked by the Boston City Hospital laboratory. A second blood culture, taken March 7, was reported positive for meningococci on March 10.

Thirty grains (2.0 gm.) of sulfanilamide was given at once, followed by 20 gr. (1.3 gm.) every 4 hours. The blood sulfanilamide level was maintained between 11.8 and 14.3 mg. per 100 cc. from March 7 until March 15, although medication was reduced gradually from March 11 because of very rapid improvement. No further chills occurred, and the temperature never rose above normal after the beginning of sulfanilamide therapy; there were no further joint pains, and the skin lesions gradually disappeared. The white-cell count gradually dropped from 18,300 on March 5 to 10,000 on March 19. Two blood cultures, after sulfanilamide treatment had begun, were reported sterile. The patient received 905 gr. (60.3 gm.) of sulfanilamide, which she tolerated well, showing only moderate cyanosis. The drug was discontinued 13 days after therapy was begun. She was discharged from the hospital on March 23 without symptoms, 23 days after admission and 37 days after onset.

One year later, the patient was in excellent health.

Summary and Conclusion

The literature on meningococcemia without meningitis is reviewed, and an additional case is reported. The diagnosis was obscure until verified by blood cultures in the third week of disease. All symptoms rapidly disappeared following sulfanilamide treatment.

The patients in the sulfonamide-treated cases of the disease thus far reported in the literature have all completely recovered promptly without sequelae.

Meningococcemia should be considered in any patient presenting symptoms of intermittent fever, unexplained rash and arthralgia.

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References

1. Salomon, H. Über Meningokoccenseptikamie. *Berl. klin. Wchnschr.* 39:1045-1048, 1902.
2. Carbonell, A., and Campbell, E. P. Prolonged meningococcemia: report of three cases. *Arch. Int. Med.* 61:646-654, 1938.
3. Schwentker, F. F., Gelman, S., and Long, P. H. The treatment of meningococcic meningitis with sulfanilamide. *J. A. M. A.* 108:1407, 1937.
4. Zendel, J. F., and Greenberg, D. Meningococcemia: treatment with sulfanilamide and prontosil. Report of two cases. *New York State J. Med.* 37:1744-1748, 1937.
5. Dimson, S. B. Chronic meningococcal septicemia treated with 2-(p-aminobenzenesulphonamido) pyridine. *Lancet* 2:424-426, 1938.
6. Craven, E. B., Jr. Chronic meningococcus septicemia. *South. Med. & Surg.* 101:367-369, 1938.
7. Long, P. H., and Bliss, E. A. *The Clinical and Experimental Use of Sulfanilamide, Sulfapyridine and Allied Compounds.* 319 pp. New York: Macmillan Co., 1939.
8. Binns, F., and Clancy, J. J. Chronic meningococcemia promptly cured by sulfanilamide. *Am. J. Dis. Child.* 57:404-408, 1939.
9. Levy, G. J. The treatment of infectious diseases with sulfanilamide. *Memphis M. J.* 12:192-197, 1937.
10. Kattwinkel, E. E. Meningococcemia. *New Eng. J. Med.* 224:685, 1941.

MEDICAL PROGRESS

NUTRITION*

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THE purpose of this review is to emphasize, not the vitamins, — important though they are, — but the phase of nutrition that relates to national welfare, both present and future, and should be familiar to all physicians. In addition, several aspects of nutrition not commonly considered in reviews on deficiency disease are presented.

A rapidly increasing literature attests that the study of nutrition has passed the purely animal stage and is already deep into its application to human physiology and pathology. A number of the recent papers on this subject are purely inspirational and emphasize the lag between the accumulation and the practical application of nutritional knowledge.[1-3] Even the economic, social and political consequences that result from adequate or inadequate human nutrition are being considered.[4-6] World War II, with its mass experiments in malnutrition, and the defense efforts have stimulated an interest in nutrition never witnessed before in this country. Indeed, adequacy of nutrition may determine the political fate of a nation, as well as the physical well-being and the morbidity and mortality of its people for a generation to come. The desire to have it favorably influence the Nation and the people becomes clearer each day.

NATIONAL NUTRITION CONFERENCE FOR DEFENSE

The progress of nutrition in this country reached a pivotal point on May 26, 1941, when over eight hundred delegates (representing every interest in this field) met in Washington to attend the three-day National Nutrition Conference for Defense, called at President Roosevelt's request. The medical profession was well represented by noted nutritional authorities. Few such national conferences have been held, and none previously to discuss nutrition. Physicians may thus judge the import of this meeting. Procedures of the conference are not yet available, but a detailed review,[7] including parts of the original manuscripts, has been published. Its scope is too vast for a complete analysis to be given. However, a few points will be presented so that its main objectives and far-reaching implications will be appreciated.

Brigadier General Lewis B. Hershey, deputy director of the Selective Service System, stated that, of 380,000 rejections for general military service, it had been estimated that perhaps one third were due either directly or indirectly to nutritional deficiencies. Paul V. McNutt, Federal Security Administrator, quoted President Roosevelt as emphasizing the present significance of the nutritional problem, as follows:

> . . . . During these days of stress the health problems of the military and civilian population are inseparable. Total defense demands manpower. The full energy of every American is necessary. Medical authorities recognize completely that efficiency and stamina depend on proper food. Fighting men of our armed forces, workers in the industry, the families of these workers, every man and woman in America, must have nourishing food. If people are undernourished, they cannot be efficient in producing what we need in our unified drive for dynamic strength. . . . The Department of Agriculture has estimated that many millions of men, women, and children do not get the foods which science considers essential.

Surgeon General Thomas Parran summed up the American food situation in this way:

> . . . . One half of our fuel — the calories we eat — is in the form of bread and sugar. Add to this the refined fats, and two thirds of our energy intake is in the form of "inert calories," which furnish fuel and nothing else. From the remaining third of our diet we must get the vitamin B complex and the minerals needed to burn up the inert calories. This is where we have been starving ourselves.

The Committee on Food Habits organized by the National Research Council will attempt by education and practical psychology to change the food habits of the public. Dr. Russell M. Wilder, chairman of the Committee on Foods and Nutrition, explained how the recent origin of scientific nutritional knowledge, the difficulty of recognizing minor clinical deficiencies and the prevalence of quackery and food fads in the nutritional field had made many physicians hesitate to apply the principles of nutrition in their practices. He ended his address with a plea to the physician to assume leadership in this field.

The conference made a number of specific recom-

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mendations to the President. Briefly, these were the use of the suggested nutritional yardstick (Table 1) as a goal for adequate nutrition; the translation of these allowances into units understandable by the laity; continued nutritional research; the education of all professional groups concerned with nutrition (that is, doctors, dentists, teachers and so forth); the education of the public in nutritional knowledge; the mobilization of any organized unit able to contribute to this campaign; the continued attack on fundamental problems of unemployment; the use of any practical device to bring foods to those otherwise unable to afford them, such as the so-called "stamp plan"; the improvement of food distribution; the encouragement of agriculture to a greater production of foods needed in abundance; the encouragement of more production for home use by rural people; and the enrichment of certain staple food products. The realization of these recommendations is certain to have a profound influence for the better on the future health of the Nation and will do much to improve the efficiency of the present defense effort. Nutritional information becomes of more value in the practice of medicine than ever before. An editorial comment in the *Journal of the American Medical Association*[8] concerning this conference is well worth reading.

The highlight of the conference, so far as the practitioner of medicine is concerned, was the promulgation by the Committee on Foods and Nutrition of the National Research Council[9] of recommended daily allowances for the various dietary nutrients (the so-called "yardstick for good nutrition"); these allowances are given in Table 1. They represent the available scientific knowledge. Nutritional authorities were willing to accept these values tentatively until standards derived from more exact data could be obtained. Foods supplying adequate thiamin, riboflavin and nicotinic acid will tend to supply an adequate amount of the remaining components of the vitamin B group. Diets adequate in protein, calcium and iron will tend to supply other needed minerals, although these are not listed. Adult allowances are given for a man weighing 154 pounds (70 kg.) and for a woman weighing 123 pounds (56 kg.), at three

TABLE 1. *Recommended Daily Allowances for Specific Nutrients.**[9]

	Energy	Protein	Calcium	Iron	Vitamin A†	Thiamin (Vitamin B_1)‡	Riboflavin	Nicotinic Acid	Ascorbic Acid‡ (Vitamin C)	Vitamin D‖
	cal.	*gm.*	*gm.*	*mg.*	*int. units*	*mg.*	*mg.*	*mg.*	*mg.*	*int. units*
Man (70 kg.)										
Moderately active	3000	70	0.8	12	5000	1.8	2.7	18	75	
Very active	4500					2.3	3.3	23		
Sedentary	2500					1.5	2.2	15		
Woman (56 kg.)										
Moderately active	2500	60	0.8	12	5000	1.5	2.2	15	70	
Very active	3000					1.8	2.7	18		
Sedentary	2100					1.2	1.8	12		
Pregnant (latter half)	2500	85	1.5	15	6000	1.8	2.5	18	100	400–800
Lactating	3000	100	2.0	15	8000	2.3	3.0	23	150	400–800
Children up to 12 years										
Under 1 year§	100/kg.	3–4/kg.	1.0	6	1500	0.4	0.6	4	30	400–800
1–3 years¶	1200	40	1.0	7	2000	0.6	0.9	6	35	
4–6 years	1600	50	1.0	8	2500	0.8	1.2	8	50	
7–9 years	2000	60	1.0	10	3500	1.0	1.5	10	60	
10–12 years	2500	70	1.0	12	4500	1.2	1.8	12	75	
Children over 12 years										
Girls										
13–15 years	2800	80	1.3	15	5000	1.4	2.0	14	80	
16–20 years	2400	75	1.0	15	5000	1.2	1.8	12	80	
Boys										
13–15 years	3200	85	1.4	15	5000	1.6	2.4	16	90	
16–20 years	3800	100	1.4	15	6000	2.0	3.0	20	100	

*Tentative goal toward which to aim in planning practical dietaries; can be met by a good diet of natural foods. Such a diet will also provide other minerals and vitamins, the requirements for which are less well known.

†Requirements may be less if provided as vitamin A; greater if provided chiefly as the provitamin carotene.

‡1 mg. thiamin = 333 int. units; 1 mg. ascorbic acid = 20 int. units.

§Needs of infants increase from month to month; the amounts given are for approximately 6 to 8 months. The amounts of protein and calcium needed are less if derived from breast milk.

¶Allowances are based on needs for the middle year in each group (2, 5, 8 and so forth) and for moderate activity.

‖Vitamin D is undoubtedly necessary for older children and adults; when not available from sunshine, it should be provided probably up to the minimum amounts recommended for infants.

Reprinted, with slight modification, with the permission of Dr. Russell M. Wilder, chairman, Committee on Foods and Nutrition, National Research Council. Copies of this chart, with explanatory notes, can be obtained from Nutrition Division, Federal Security Agency, Washington, D. C.

levels of physical activity, and should be proportionately increased or decreased for larger or smaller persons. Allowances for the vitamin B group are proportional to the calorie intake, and apply to healthy persons; disease may alter them considerably. It is of interest that the protein requirement does not increase with activity in adults. It is increased during pregnancy and lactation, and for children and adolescents. Calcium requirements are discussed in detail elsewhere in this paper. The committee expects nutritional workers to translate these scientific terms into appropriate quantities of foodstuffs available in their own locality and to meet special situations.

The various nutrients provided for in these allowances, with the exception of vitamin D, can be obtained through a diet of natural foods or foods enriched according to the committee's recommendation. Translation of these allowances into a daily dietary pattern of actual foods is given in Table 2. This is an excellent list for the physician

TABLE 2. *Dietary Pattern Suggested by the Committee on Foods and Nutrition, National Research Council.*[9]

FOOD	AMOUNT
Milk	Adults, 1 pint; children, 1½ pint to 1 quart
Egg	Three or four times per week
Meat	One serving (30 gm. at 1 year, up to 90 gm. for adults)
Vegetables	Two servings (one green or yellow)
Fruit	Two servings (one citrus or tomato)
Potato	One or more servings
Butter or fortified oleo	100-500 calories
Whole grain or enriched cereal and bread	At least half the intake
Sugar, fat and so forth	To complete the caloric requirement

to keep in mind when he attempts to evaluate the adequacy of his patient's diet. It is well to note that half the caloric intake is of whole grain or enriched cereal and bread, and that specific minimums for milk intake are given.

NUTRITIONALLY IMPROVED OR ENRICHED FOODS

The introduction of steel-roller milling of wheat some seventy years ago cheapened the cost of producing white flour and resulted in its displacement of whole-meal flour. Nutritional loss to the public resulted, inasmuch as white flour contains almost no vitamin E and less protein, calcium, phosphorus, iron, vitamin B complex and carotene than whole-meal flour.[10] White flour has been used not only for bread, but for cakes, pies, gravies, sauces, crackers and so forth, and contributes 25 per cent or more to the average daily caloric intake. A comparison of the ingredients of nutritional value of white flour with whole-wheat flour is given in Table 3. A further comparison of this table with the requirements listed in Table 1 demonstrates the nutritional inadequacy of white flour. The superior taste and appearance of white bread originally dictated this change. The nutritional error thus committed did not become apparent until about 1920, and only recently has its full import been appreciated by nutritional experts.[1, 10, 11] In the meantime, several generations

TABLE 3. *Average Values for Whole-Wheat, White and Enriched Flour.*

PRODUCT	CALCIUM	PHOSPHORUS	IRON	THIAMIN	RIBOFLAVIN	NICOTINIC ACID	VITAMIN D
	mg./lb.	*mg./lb.*	*mg./lb.*	*mg./lb.*	*mg./lb.*	*mg./lb.*	U.S.P. *units*
Whole-wheat flour	240	1,700	18.0	2.04	1.13	12.3	—
White flour	72	460	4.5	0.23	0.18	3.7	—
Enriched flour*							
Minimum enriched	500†	—	6.0	1.66	1.2	6.0	250†
Maximum enriched	2,000†	—	24.0	2.50	1.8	9.0	1,000†

*Composition of flour enriched according to the definition and standard proposed by the United States Food and Drug Administration.

†Optional ingredients, at least for the present.

This tabulation originally appeared in a report of the Council on Foods and Nutrition, American Medical Association,[19] and is reproduced with the permission of the publisher.

have accepted white flour as a major item in their diet and have become accustomed to its use.

Most of the sugar used in this country is refined and hence devoid of minerals and vitamins. The daily per-capita consumption of sugar is said to average about 155 gm., which represents 600 calories, or one fourth of all the calories of the diet.[1] Last year, only one fourth of the margarine in the United States was fortified with vitamins.[1] Lard and polished rice, likewise poor vitamin sources, are used extensively.

It is a nutritional fallacy to teach that the balance of the American diet, even if good natural foods are used, will compensate for this 50 per cent or greater caloric content lacking in minerals and vitamins. Reference to Table 2, which lists a truly adequate diet, makes this point clear. Each food is expected to carry its own weight in contributing to the adequacy of the total diet.

The eating habits of the American public are now so well established that a worth-while change, although not impossible, would be slow. Some favor education of the public to the use of natural foods.[12] The present world crisis makes it imperative that this country secure, as rapidly as possible, the benefits to accrue from application of nutritional knowledge. To this end, fortification or enrichment of foods with nutritional ingredients lost in the manufacturing process is considered a worth-while solution.[13-15] Wilder[1] has discussed the inadequacies of solving this problem by urging the public to consume vitamin and mineral pills.

Fortification of food is by no means a new or

untried procedure. Over fifteen years ago, salt was fortified with iodine in the endemic goiter regions, with excellent prophylactic results.[2] Fortification of foods with vitamin D has reduced the incidence of rickets.[2] Fortification of margarine with vitamins A and D was made compulsory in Denmark years ago[1] and has already been used with some of the margarine sold in this country.

The possibilities of enrichments of flour and bread have aroused much interest and comment, as well as some criticism both in this country[1, 7, 11, 13] and in England.[16–18] The Council on Foods and Nutrition of the American Medical Association has recently submitted a detailed report on this subject.[19] There is much to be said in favor of using only natural unrefined foods.[12] However, many objections have arisen to this proposal. In brief, time would be required to change the people's food habits; many do not like the taste or appearance of dark bread; others must avoid the effect of its roughage on their gastrointestinal tract; the baking qualities are not so good as those of white flour; whole-meal flour does not keep so well; and much money is now invested in milling equipment for preparing white flour.[1, 2, 7, 10, 11] One may expect to see the fortification of flour practiced extensively in the future. The British have already fortified their white flour with calcium, iron and thiamin.[16, 18] Fortification of flour is more advantageous than direct fortification of bread, since flour is widely used for other purposes besides bread.

Table 3 gives the average composition of whole-wheat and white flour and, for comparison, the minimum and maximum degrees of enrichment of flour according to the definition and standard proposed by the United States Food and Drug Administration. In principle, this has been endorsed by the Council of Foods and Nutrition of the American Medical Association and by the Committee on Food and Nutrition of the Division of Medical Sciences of the National Research Council. The reason for each figure given is discussed in detail in the council's report.[19] Briefly, the council sponsors "fortification with a limit, that limit being the content of the natural or unprocessed foods." Standards for enriched bread as suggested by the Committee on Food and Nutrition of the National Research Council are given in Table 4. Thus, white bread, with no change in taste or appearance, will approach whole-wheat bread in nutritive qualities. New milling technics, which preserve more of the original nutritive ingredients of wheat and still produce a white flour, have been perfected, and will be further improved with time. The vitamin B complex of bread could also be fortified with more nutritious forms of yeast.[19]

Wilder[1] has made several suggestions. If each average daily per-capita portion of sugar (155 gm.) were fortified with slightly more than 30 gm. of skimmed-milk solids, the average American diet would be improved by the addition of the equivalent of a pint of skimmed milk. The edible fats, margarine and lard, can be fortified with vitamins A and D. Ascorbic acid is sensitive to oxidation and heating and is therefore less well suited for fortification. However, citrus fruits, tomatoes and potatoes — good to fair food sources of vitamin C — are plentiful in this country. Irradiation of food, to increase its vitamin D content, is already widely practiced. The many suggestions for fortifying foods with calcium are discussed below.

TABLE 4. *Suggested Standards for Enriched Bread.*

ENRICHMENT	CALCIUM	PHOSPHORUS	IRON	THIAMIN	RIBOFLAVIN	NICOTINIC ACID
	mg./lb.	*mg./lb.*	*mg./lb.*	*mg./lb.*	*mg./lb.*	*mg./lb.*
Minimum	300*	—	4.0	1.0	0.8	4.0
Maximum	1200*	—	16.0	2.0	1.6	8.0

*Optional.

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NUTRITIONAL ASPECTS OF CALCIUM

In contrast to the many publications dealing with vitamins is the comparatively modest but nevertheless important literature concerned with the nutritional aspects of calcium. With almost no exception, these papers stress the frequent inadequacy of this substance in the American and English diet.[20–23] In fact, the investigative methods of one of the few recent papers[24] to contradict this point of view were immediately criticized, and its results discounted.[25–27] Although realizing the significance of an adequate calcium intake for infants and young children, few physicians have paid much attention to the calcium intake of adults. The metabolism of calcium, phosphorus and vitamin D is closely related and interdependent. Phosphorus is present in many foods, so that diets are rarely deficient in this substance. Foods adequate in protein contain sufficient phosphorus. In fact, no specific mention of phosphorus requirements was given at the National Nutrition Conference (Table 1). Practically none of the common foods are adequate in vitamin D. Infants and children now almost universally receive fish-liver oil, viosterol or irradiated foods to supply this deficient vitamin. And its use during pregnancy and lactation is rapidly increasing. Adults

with no opportunity for exposure to sun may require supplementation of their diet with vitamin D (Table 1).

Of the aforementioned triad, calcium is the substance that is likeliest to be deficient in the average diet; rarely is an attempt made to remedy this fault.

Of the total calcium content of the body, 99 per cent is contained in the bones, none in the red blood cells, a small amount in tissue fluids and 9.5 to 11.5 mg. in each 100 cc. of blood serum.[28, 29] The necessity of the blood calcium for normal neuromuscular irritability, clotting of blood and so forth is too well known to require comment.

Active adults with normal endocrine and renal function, an adequate supply of vitamin D and proper intestinal absorption maintain a normal blood-calcium level regardless of the adequacy of the dietary calcium; calcium is removed from the trabeculae of the bones when the calcium balance is negative and stored when the supply is great.[28] Urinary and stool excretion of calcium continues, even when the dietary intake of calcium is low or absent. The influence on bone metabolism of long-continued dietary calcium deficiency, with resultant negative calcium balance, has aroused much interest in recent years.[30–34] Vitamin D and a sufficient amount of phosphorus are essential for the proper metabolism of calcium, as is normal parathyroid function. The presence of hydrochloric acid, sucrose, lactic acid and citric acid in the gastrointestinal tract favors calcium absorption.[22, 35] Alkalies, excess fats, excess phosphates, oxalic acid (present in leafy vegetables), maltose and starch interfere with its absorption.[22] The phytic acid of cereals was formerly believed to immobilize calcium.[35] However, in more recent studies, calcium phytate proved to be readily absorbed.[36] By interfering with the utilization of vitamin D, the ingestion of mineral oil in growing dogs has been found to result in poor retention of both calcium and phosphorus, with the development of rickets.[37] This may or may not be of clinical significance. The ration used contained 5 to 10 per cent mineral oil, proportionally more than is likely to be used by human beings. All this emphasizes the complexity of the problem of calcium absorption and the need for a safe margin over the amount estimated for maintenance requirements. At best, only 20 to 30 per cent of calcium ingested by adults and older children is utilized.[35]

Milk and cheese are the only good sources of calcium in the diet, and in their absence it is exceedingly difficult to fill the calcium need through food alone.[22] The inadequacy of calcium in other foods is well illustrated in a table prepared by Bernheim.[22] To secure 0.70 gm. of calcium daily from any other single food, it would be necessary to eat 3.2 lb. of beans, 7.3 lb. of white bread, 5.5 lb. of brown bread, 11.0 lb. of butter, 1.5 lb. of cauliflower, 27.5 lb. of corn, 20 eggs, 2.3 lb. of oatmeal, 17.0 lb. of potatoes, 4.9 lb. of oranges, 26.4 lb. of lean meat, 14.7 lb. of fish and so forth. Furthermore, the oxalic acid present in some leafy vegetables prevents adequate absorption by the formation of insoluble calcium oxalate in the intestinal tract.

A quart of milk contains slightly more than a gram of calcium (1.16 gm.) — a useful figure to commit to memory. An economical source of milk looms large as a factor in arranging for an adequate supply of calcium in diets of persons in the low-income group.[38] Koehne[39] has some interesting recommendations in this regard. A 1¼-in. (3.2-cm.) cube (30 gm.) of yellow cheese may be substituted for half a pint of milk. This contains about 0.25 gm. of calcium. Skimmed milk or butter-milk is the equivalent of whole milk in calcium and protein, but not, of course, in fat or the fat-soluble vitamins, and is much cheaper.[39] Both are excellent sources of calcium for persons attempting to lose weight. Evaporated milk is the equivalent of whole milk in calcium content and is less expensive. Dry skimmed milk (dry milk solids) has the food value of whole milk, except for the fat, and is cheaper. One quarter of a pound (120 gm.) of dry skimmed milk, diluted with water, makes a quart of fluid skimmed milk. Milk used in cooking, desserts made from milk, ice cream, because of milk content, and so forth, add to the calcium content of the diet. For all practical purposes, a check on the calcium content of a patient's diet concerns information on the use of these items.

From the evidence already presented, the frequency of calcium deficiency in the American diet becomes understandable. Serious consideration has been given to various plans to increase the calcium content of staple foods. The supplementation of white flour with calcium, to a maximum of 2000 mg. per pound (Table 3), is one proposal. The addition of milk solids to cane sugar is another.[1] The British have already added 7 ounces (210 gm.) calcium carbonate (creta praeparate *B.P.*) to each 280-pound sack of white flour used in the preparation of their so-called "war loaf." Fortification of breakfast cereals with calcium is another suggestion. For example, Pierce and others[40] found that when part of the milk calcium of an adequate diet fed to children was re-

placed by an equivalent amount supplied by tricalcium phosphate in a fortified cereal, utilization as measured by retention was equally good from milk and cereal.

Furthermore, direct supplementation of the diet with one of the calcium salts is entirely possible if an adequate supply of food calcium is lacking. A number of studies indicate that this substitution is practical on an extensive scale. Aykroyd and Krishman[41] during a four-month period gave children (ages two and a half to seven) in a nursery school in South India 0.5 gm. of calcium lactate daily. The children showed greater increases in weight, height and general well-being than a control group of children in the same school who did not receive the supplement. These authors recommend that calcium salts be used as a partial substitute for milk when the latter cannot be obtained. Gaunt and his associates[42] had previously shown that improvement exhibited by a large colony of rats (reared for generations on an average diet eaten by a working-class community in Scotland) when greens and milk were added to this diet could be duplicated in large part by adding mineral supplements of calcium and phosphorus. In human practice, increased consumption of milk was recommended as the best means of improving the diet whenever it was possible.

Gunderson[43] discusses the economics of the use of calcium salts. Precipitated calcium carbonate is listed as the most economical source, calcium gluconate as the most expensive. Calcium triphosphate, calcium phosphate (bone meal), calcium diphosphate, calcium monophosphate, calcium citrate and calcium lactate range between these in this order.

The calcium requirements for human beings have been worked out by means of calcium and phosphorus studies, the presence and degree of positive or of negative calcium balance for various levels of calcium intake being determined. In addition, the rate of growth and weight of the skeletal structure has been considered. Leitch[44] reviewed the literature dealing with this subject. By such means, the minimal or maintenance requirement for calcium is determined. Optimal requirements used for clinical purposes are determined by adding 50 per cent to this minimal level to allow for possible difficulties in utilization (as was noted above in the discussion on the absorption of calcium).

For many years, Sherman's[23] estimate of 0.45 gm. of calcium as the minimal and 0.70 gm. as the optimal daily requirement for an adult weighing 154 pounds (70 kg.) was the accepted standard. Owen[45] found 0.52 gm. to be the minimum, whereas Leitch,[44] from an extensive survey, gave 0.55 gm. as a minimum. The optimal daily allowance for calcium as recommended by the Committee on Foods and Nutrition of the National Research Council is given in Table 1: 0.8 gm. for adult men and women, 1.5 gm. during pregnancy, 2.0 gm. during lactation, 1.0 gm. for small children, and 1.3 to 1.4 gm. from puberty until growth is completed.

The greater need for calcium during the years of growth, pregnancy and lactation should be constantly kept in mind. The difficulty of sustaining lactating women in a positive calcium balance has been emphasized.[46] The calcium problem in obstetrics has been discussed by Bear[47] and by Mendenhall and Drake.[48] The diet during puberty needs special attention. In a survey in Toronto among families able to supply a reasonably good diet, the lowest intake of calcium and milk was found in the girls in their teens, explainable on the current desire of girls to be slim.[49] McHenry urges that this group be educated to realize that an adequate knowledge of nutrition allows one to avoid obesity and still to be properly fed. Skimmed milk or dry milk solids may be substituted for whole milk if the fear of obesity causes the latter to be omitted from the diet.

What ill effects are to be expected when adults live for years on a diet deficient in calcium? Many recent papers[30, 32, 34, 44] have attempted to correlate the considerable incidence of osteoporosis among persons past middle life with this factor. Nervous irritabilities have likewise been attributed to this cause.[30] However, the cause of senile osteoporosis is by no means settled. Among the possible explanations are: long-continued dietary calcium deficiency, with negative calcium balance and gradual demineralization of the skeleton[34]; deficiency of vitamin D[33]; inability to absorb mineral salts from the gastrointestinal tract with advancing years[33]; the presence of achlorhydria in old age[32]; atrophy of bone due to disuse as the result of restricted physical activity in old age[50]; and senescent changes.[50]

Albright and his co-workers[50] have described postmenopausal osteoporosis, a form of bone disease often confused with senile osteoporosis, and attribute it to the endocrine changes following the menopause. A beneficial effect of estrogen therapy on the retention of calcium in this condition was noted. They consider osteoporosis a disease in which the osteoblasts are primarily deficient in laying down osteoid tissue, and believe that a negative nitrogen balance may interfere with osteoblastic activity in laying down the necessary organic matrix. Such a factor could well be present

in old age. Adequacy of protein in the diet thus becomes a factor to be considered in the etiology of senile osteoporosis.

Owen, Irving and Lyall[34] made calcium balance studies of 7 male patients over seventy years of age; 4 of them manifested osteoporosis by roentgenographic examination. Three were in calcium equilibrium with intakes of only 0.3 gm. calcium. The authors believe that their results suggest adaptation by the body to the continued smaller calcium intake by a lower rate of calcium turnover and a lessened reserve of calcium in the skeletal stores; they conclude that prolonged nutritional calcium deficiency may result in generalized osteoporosis in elderly patients. Leitch[44] subscribes, in part at least, to the theory that senile osteoporosis is due to prolonged calcium deficiency. The study of Adams, Boothby and Snell[51] indicates that treatment of senescent osteoporosis with calcium salts can convert a negative calcium balance to a positive one and thus store calcium and phosphorus. Their subject, a sixty-five-year-old woman with osteoporosis, stored over a nineteen-week period 29.3 gm. of calcium and 13.3 gm. of phosphorus, a ratio of 2.2:1 — or the ratio of these substances in bone.

These studies seem to indicate that adequate calcium, protein and vitamin D nutrition throughout life may prevent the development of osteoporosis in old age. Furthermore, treatment of senile osteoporosis with a diet adequate in protein and calcium, supplemented with calcium and phosphorus salts and vitamin D, has some rationale as a therapeutic procedure. To be successful, it will probably have to be continued for a long time.

The nature and the amount of the dietary intake of calcium, aside from its purely nutritional aspects, are often of diagnostic or therapeutic interest in the practice of medicine. For example, in using the Sulkowitch reagent to test for calcium in the urine, one should remember that normal persons may show excess urinary calcium shortly after drinking a large amount of milk.[29] This may be confused with hypercalcinuria due to disease. Albright,[29] in discussing the treatment of hypoparathyroidism, stresses the need for a high intake of calcium and a low intake of phosphorus, but adds that, in spite of its high calcium content, milk is contraindicated because it is likewise high in phosphorus. Persons with prolonged recumbency and immobilization of the body because of injury or disease often have hypercalcinuria due to demineralization of the skeleton, with the formation of renal calculi. Carlson and Ockerblad[52] point out that the use of much milk, the basis of most sickroom diets, often leads to excessively high calcium intakes, which become an additional factor to be considered under such circumstances in explaining the calculus diathesis. Barney and Jones[53] suggest that ingestion of excessive amounts of milk and cheese, especially when the urine is alkaline, may, by precipitating calcium phosphate in the urine, be a factor in the formation of calculi in the urinary tract. Kempster and others[54] recommend that persons allergic to milk secure their daily calcium requirement as dicalcium phosphate, with a percentage utilization equal to the calcium in milk. Albright[29] has emphasized the fact that the characteristic bone changes of hyperparathyroidism may be lacking if the patient's diet has contained sufficient calcium to balance the excess urinary calcium loss. Such persons are invariably heavy milk drinkers. Diagnosis then rests on the chemical findings in the blood, the presence of renal calculi, systemic symptoms and so forth.

Nutrition in Old Age

Many publications have appeared in recent years stressing the importance of the study of disease in old age. In fact, the rise of the specialty of geriatrics — the old-age counterpart of pediatrics — is foreseen,[55] a possibility by no means unlikely in view of the increasing proportion of older people in this country's population. Official cognizance of the senescent individual in the national life and economy was recently taken by the United States Public Health Service with the establishment of a Unit of Gerontology at the National Institute of Health.[56] Under the editorship of Cowdry,[57] the known facts concerning the aging process have been reviewed.

Sherman[58] believes that the nutritional knowledge already available will, if properly applied, "'add life to our years,' and . . . add years to our lives." Food and nutrition have now been accorded a place, along with heredity, in the control of longevity. The praiseworthy results of the increasing appliance of the nutritional principles in the practice of pediatrics are too well known to need any comment. One already finds cautious suggestions[1, 25, 59] that long-continued inadequacy of diet may be a factor in the early development of degenerative diseases. Naturally, to be truly effective, such dietary principles must be applied early in life. Harris[60] aptly emphasizes the fact that the effective practice of geriatrics must begin where the pediatrician leaves off. The effects of a lifetime of unhygienic habits and an incorrect diet cannot be righted, once old age is reached. The practitioner of medicine — the family doctor — is thus entrusted with the promulgation of this thesis. An inquiry into a per-

son's habits of eating and recommended dietary changes, as the circumstances require, may well become a routine part of the annual health check-up now being widely recommended to the public by many agencies.

Diminution of appetite is common in old age, and its causes and remedies have been discussed by Meyer.[61] This, coupled with the fact that many elderly people because of loss of teeth and inadequate artificial dentures are unable to chew properly, frequently marks the onset of a poor dietary regime in old age. The latter cause is commonly responsible for the clinically detectable deficiencies noted in old people studied on the medical wards of the Boston City Hospital.[62] Meyer and his co-workers[63] found that old people have less salivary secretion of ptyalin than young adults, with resultant deficiency of starch digestion in the mouth and stomach. Whereas 50 gm. of white bread is easily digested in the mouth and stomach of young people, only 0.5 gm. is digested by old people.[63] Masticatory difficulties in old age often necessitate a soft diet, relatively high in carbohydrates and low in protein. However, the same workers[64, 65] found in a later study that the total intestinal digestion of carbohydrates was not markedly disturbed, because the pancreatic amylase, although slightly subnormal, was sufficient to complete this digestive process. They occasionally noted, in fact, abnormally high values for this pancreatic enzyme in the age group from eighty-one to one hundred years. These levels were considered to be possibly compensatory for the lowered salivary ptyalin of old age. Both proteolytic enzymes (pepsin and trypsin) were found to be diminished in old age, but they concluded that the concentration was adequate to meet the requirements of the usually decreased protein intake. They admit, however, that some old people consume large quantities of protein, with apparently normal digestion. They conclude their paper by stressing the fact that such studies may be helpful in rationalizing the dietary management of old persons.

The incidence of achlorhydria is known to increase with advancing age.[66] The influence of achlorhydria on the absorption of various substances in the diet and their utilization by the body may be important. Its interference with the absorption of iron has been established. Less is known of its influence on the absorption of fractions of the vitamin B complex and other dietary factors. Leitch[44] comments on the need for more knowledge of its relation to the absorption of calcium, a subject worthy of investigation, in view of the frequency of osteoporosis in old age.

Interference with eating in old age commonly results from digestive symptoms. Meyer[61] stresses their frequency, and emphasizes that cardiac, renal and hematologic disorders, all particularly common at this time of life, may be factors in producing such symptoms, apart from diseases primary in the gastrointestinal tract. Physiologic changes incident to the aging process are undoubtedly additional factors in causing such symptoms. All this serves to emphasize again that maintenance of adequate nutrition is often more difficult in old age than in early life.

Tuohy[67] found that undernutrition in the aged was more frequently the result of perverseness of appetite than economic adversity. He noted that old people often limit their diet because of faulty advice or inherent fear of eating adequately. The *Journal of the American Medical Association*[68] has commented editorially on this subject.

Owen[45] and Robertson,[69] from calcium balance studies on old men, found their requirements to be much the same as those of young adults, with a further similarity that they readily retained calcium and phosphorus after depletion. Increasing age did not offset long subjection to a diet low in calcium.

The significance of long-continued negative calcium balance on the genesis of senile osteoporosis has already been discussed.

The average 10 per cent reduction in the basal metabolic rate of old age[70] and the lowered physical activity indicate the need for reduction in caloric intake. The adverse influence of obesity on longevity is well recognized. The diet of old age must therefore be planned to avoid this factor and eliminate it if it is already present.

Vitamin deficiencies, especially of minor degree or with atypical manifestations, are common in old age.[67] Tuohy[67] remarks that gastrointestinal atony may respond to the use of thiamin. Mental changes often ascribed to the aging process may be due to nicotinic acid deficiency.[71]

Piersol and Bortz[72] suggest the use of liver twice weekly, in addition to iron-rich foods, to maintain the red-cell count at a normal level; milk is urged as an ideal food for old age. They also comment that a minimum fat content is in order. Horn[73] likewise considers fats to be the least of the dietary essentials of old age. Tuohy[74, 75] extols the high-protein diet in old age as protective against inadequate hematopoiesis and, indirectly, liver insufficiency. He also urges a freer diet and less fear of food with old people.[67] Barowsky[76] reports that milk fortified with minerals and vitamins was well tolerated by a group of 30 senile persons. Tuohy[67] reports that arteriosclerotic persons often

tolerate several light meals better than a smaller number of heavy ones.

One may conclude from these papers that persons in the old age group can often support an adequate diet. Such a diet should be of low-caloric content, with a minimum of fat, and adequate in protein; it should contain liver and iron-rich foods and, above all, milk. The last may be given as skimmed milk if the fat content is to be avoided. Adequate intake, if necessary by supplementation, of all the vitamins is much to be desired. Since old people have but little exposure to sun, the addition of vitamin D should not be overlooked. Smaller and more frequent meals are often required. If the teeth are absent, especial care is needed to prevent inadequacies of the diet. Under such circumstances, milk becomes of even greater benefit as a primary food. Osteoporosis of old age may be preventable under such a regime.

Miscellany

Bourne's[77] book, *Nutrition and the War*, an English publication, is typical of several that attempt to educate the public in the essentials of nutrition and thus to prepare them to make the most nutritionally of every food, should the supply and variety be curtailed by war conditions. Familiarity with such material will enable physicians to give dietary advice in terms that the average layman can appreciate and understand. American physicians are not faced with the practical realities of this problem as their British colleagues are. The papers by Booher[78] and Koehne[39] give some excellent practical advice on the economic aspects of diets as related to conditions in this country.

Orr[79] discusses a hypothetical wartime diet for the general population of England that illustrates the possibility of making a satisfactory diet from a small number of foods, many of which could be produced in England. Of interest is the fact that this limited diet would be more adequate than the prewar diet of the poorest 10 per cent of the population. The study points out that all the nutrients required by the body can be obtained from a few foodstuffs. This wartime diet consists of a daily ration of 0.6 pint (300 cc.) of milk, 6 ounces (180 gm.) of vegetables, 16 ounces (480 gm.) of potatoes and 2 ounces (60 gm.) of oatmeal, — as protective foods, — and 11.8 ounces (350 gm.) of bread, 1.8 ounces (55 gm.) of fats and 1 ounce (30 gm.) of sugar — as energy-yielding foods. An important objective of such a diet is to supply protective foods first, then as many energy-yielding foods as are required to complete the desired caloric intake. Restrictions, if necessary, should apply to the latter first. Heavy work and army duty would, or course, require the above diet to be increased.

Drazin[80] reviews representative examples of diets from various parts of the world to illustrate that monotony in diet is not detrimental to good health provided it is adequate from a nutritional viewpoint. As advantages for such a diet, he lists inexpensiveness, less trouble in preparation and less conduciveness to overeating, with resultant obesity and other metabolic disorders. Such statements are reassuring in the event that the variety of foods should be curtailed because of war conditions.

Except for iodine, which is required for proper thyroid function, and possibly copper, the significance of the so-called "trace elements" in the diet is not well established. Evidence indicates that they may be indispensable constituents of intracellular enzyme systems. Underwood,[81] Shohl[82] and Daniel[83] recently reviewed this subject and have listed detailed bibliographies. No direct clinical application to nutrition is in order at this time.

The influence of heating,[11, 84] canning,[11] and quick freezing[85] on the nutritive value of foods has continued to receive attention. It is of interest that the values recommended by the National Research Council (Table 1) refer to the amount of each factor actually eaten and make no allowance for extensive losses in cooking.[9]

The soybean is a new addition to the dietary of this country and is gaining rapidly in popularity.[80, 86] It is an unexcelled substitute for meat, its 36.5 per cent protein being of a variety closely resembling animal protein. It also contains about 20 per cent fat and 20 per cent carbohydrates.[80, 86] Soybean flour in any proportion up to 30 per cent can be used with white or whole-wheat flour.[86] The Germans are reported to be using it extensively in various forms — the so-called "Nazi food pills" — as an army ration.[87]

Bourne[88] discusses the "satiety value" of foods and points out that it is no indication of their nutritional value. Hunger is rapidly satisfied by sugar, butter, fatty foods, milk, potatoes, meat and eggs, but poorly satisfied by bread, green vegetables and nonfatty fish. As is well known, satisfaction of "hollow hunger" is no guarantee of good nutrition. It must, however, not be neglected in planning any dietary regime. Hungry people are neither content nor efficient.

Jokl and Cluver,[89] in a comparative study of the growth of physical efficiency of children from poor homes as contrasted with those from economically better situated homes, found no difference in the prepubertal age group but a striking difference in

favor of the latter after puberty. They concluded that, in the absence of true clinical deficiency, undernutrition of lesser degrees did not impair the growth of physical efficiency in the early years of life. However, the additional strain occasioned by bodily changes at the time of puberty caused a distinct lessening of the growth of physical efficiency unless the quality of the diet was improved. Table 1 shows the increased nutritional requirement at puberty suggested by the Committee on Foods and Nutrition of the National Research Council. Physicians responsible for the care of children should impress parents with the necessity of this dietary change at the time of puberty.

Many physicians find it difficult to avoid loss or interruption of sleep, long hours of work, nervous tension and improper care of their own minor ailments. However, adequate nutrition is within the grasp of each one. Olmsted[90] has written an interesting paper concerning the diet of the doctor. He believes that physicians who have good nutritional habits are sound advisers to their patients on this matter, and it affords them at least one opportunity to practice what they preach.

Sinclair[91] has reviewed the nutritional significance of fat in the diet. Reduction of fat in the diet when the caloric value is obtained mostly from crude high-carbohydrate foods — a situation common in Europe today — results in premature hunger and a reduced capacity to do sustained work. Wilder[92] also discusses the reality of "fat hunger." The per-capita consumption of fat in the occupied European countries is now less than 30 gm., — less than one quarter of the prewar level, — for the German people 60 gm. and for the German soldier 90 gm. The fat supply is ample in this country.

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References

1. Wilder, R. M. Nutrition in the United States: a program for the present emergency and the future. *Ann. Int. Med.* **14**:2189-2198, 1941.
2. Elvehjem, C. A. Diet, health and defense. *Ohio State M. J.* **37**:741-746, 1941.
3. Parran, T. Health and medical preparedness. *J. A. M. A.* **115**:49-51, 1940.
4. Gregory, R. Nutritional science and its social aspects. *Nutrition Abstr. & Rev.* **7**:1-5, 1937.
5. Orr, J. B. The physiological and economic bases of nutrition. *J. Roy. Inst. Pub. Health & Hyg.* **2**:661-676, 1939; **3**:9-24, 37-51, 1940.
6. *Idem*: Trends in nutrition. *Brit. M. J.* **1**:73-77, 1941.
7. Wilson, M. D., McNutt, P. V., Wilder, R. M., Sherman, H. C., Hershey, L. B., Wickard, C. R., Wallace, H. A., Berle, A. A., Jr., Perkins, F., Elliott, H., and Parran, T. Food for a stronger America. *Survey Graphic* **30**:377-400, 1941.
8. Editorial: National nutrition. *J. A. M. A.* **116**:2854, 1941.
9. Committee on Foods and Nutrition, National Research Council: *Recommended Dietary Allowances.* 5 pp. Washington: Nutrition Division, Federal Security Agency, 1941.
10. Copping, A. M. The nutritive value of wheaten flour and bread. *Nutrition Abstr. & Rev.* **8**:555-566, 1939.
11. Morgan, A. F. Nutrition and defense. *Am. J. Digest. Dis.* **8**:156-160, 1941.
12. Sebrell, W. H. The public health aspects of the fortification of foods with vitamins and minerals. Milbank Mem. Fund Quart. **17**:241-247, 1939.
13. Rogers, L. J. Fortification in a general program for better nutrition. *Milbank Mem. Fund Quart.* **17**:230-240, 1939.
14. Morgan, A. F. The fortification of foods with vitamins and minerals: the basic nutrition principles. *Milbank Mem. Fund Quart.* **17**:224-229, 1939.
15. Mackenzie, J. B Enriched bread: an answer to malnutrition. *J. Am. Diet. Assoc.* **17**:650-655, 1941.
16. National flour. *Lancet* **1**:703, 1941.
17. Foreign letter: Criticism of the war loaf. *J. A. M. A.* **115**:1903, 1940.
18. Foreign letter: Government decides to fortify white bread. *J. A. M. A.* **116**:1175, 1941.
19. Report of the Council on Foods and Nutrition: Nutritionally improved or enriched flour and bread. *J. A. M. A.* **116**:2849-2853, 1941.
20. Borsook, H., and Halverson, W. L. Nutrition and health in Pasadena. *Am. J. Pub. Health* **30**:895-900, 1940.
21. Stiebling, H. K. Dietary levels in the United States. *J. Nutrition* (Supp.) **19**:21, 1940.
22. Bernheim, A. R. Calcium need and calcium utilization. *J. A. M. A.* **100**:1001-1004, 1933.
23. Sherman, H. C. Calcium and phosphorus requirements of human nutrition. In *Food and Life: Year book of the United States Department of Agriculture*, 1939. 1165 pp. Washington: Government Printing Office, 1939. Pp. 187-197.
24. Harris, I., Ireland, J. R., and James, G. V. Optimum calcium requirement. *Brit. M. J.* **1**:49, 1941.
25. Leitch, I. Letter to Editor. *Brit. M. J.* **1**:291, 1941.
26. Robertson, J. D. Letter to Editor. *Brit. M. J.* **1**:292, 1941.
27. McCance, R. A. The metabolism, excretion and human requirements of calcium. *Brit. M. J.* **1**:276, 1941.
28. Farquharson, R. F. Calcium requirements of the normal individual. *Canad. M. A. J.* **39**:280-282, 1938.
29. Albright, F. The parathyroids: physiology and therapeutics. *J. A. M. A.* **117**:527-533, 1941.
30. Wilder, R. M. Nutritional problems as related to national defense. *Am. J. Digest. Dis.* **8**:243-245, 1941.
31. Black, J. R. Senile osteoporosis of the spine. *Proc. Staff Meet., Mayo Clin.* **15**:619-622, 1940.
32. Meulengracht, E. Osteomalacia of the spinal column from deficient diet or from disease of the digestive tract. I. From deficient diet. *Acta med. Scandinav.* **101**:138-156, 1939. II. Osteomalacia achylia. *Ibid.* **101**:157-186, 1939.
33. Editorial: Senile osteoporosis. *J. A. M. A.* **112**:434, 1939.
34. Owen, E. C., Irving, J. T., and Lyall, A. The calcium requirements of older male subjects with special reference to the genesis of senile osteoporosis. *Acta med. Scandinav.* **103**:235-250, 1940.
35. Editorial: Calcium requirements. *Brit. M. J.* **1**:281, 1941.
36. Krieger, C. H., Bunkfeldt, R., and Steenbock, H. Cereals and rickets: calcium phytate as a source of calcium. *J. Nutrition* **20**:15-18, 1940.
37. Smith, M. C., and Spector, H. Calcium and phosphorus metabolism in rats and dogs as influenced by the ingestion of mineral oil. *J. Nutrition* **20**:19-30, 1940.
38. Eichelberger, M. The importance of economical milk in human nutrition. *Am. J. Pub. Health* **30**:169-174, 1940.
39. Koehne, M. Adequate diets at low cost. *Ohio State M. J.* **36**:762-769, 1940.
40. Pierce, H. B., Daggs, R. G., Meservey, A. B., and Sinicox, W. J. The retention of calcium and phosphorus by pre-school children. *J. Nutrition* **19**:401-414, 1940.
41. Aykroyd, W. R., and Krishman, R. Effect of calcium lactate on children in a nursery school. *Lancet* **2**:153-155, 1938.
42. Gaunt, W. E., Irving, J. R., and Thomson, W. Calcium and phosphorus deficiencies in a poor human dietary. *Brit. M. J.* **1**:770-773, 1938.
43. Gunderson, F. L. Nutritional economics of dietary calcium. *Am. J. Pub. Health* **27**:570-574, 1937.
44. Leitch, I. The determination of the calcium requirements of man. *Nutrition Abstr. & Rev.* **6**:553-578, 1937.
45. Owen, E. C. The calcium requirement of older male subjects. *Biochem. J.* **33**:22-26, 1939.
46. Rabinowitch, I. M. Nutritional requirements of the mother during lactation. *Canad. M. A. J.* **39**:76-79, 1938.
47. Bear, J. The calcium problem in obstetrics. *Virginia M. Monthly* **67**:553-557, 1940.
48. Mendenhall, A. M., and Drake, J. C. Calcium deficiency in pregnancy and lactation. *Am. J. Obst. & Gynec.* **27**:800-807, 1934.
49. McHenry, E. W. Some observations on Canadian nutrition. *Canad. Pub. Health J.* **31**:584-588, 1940.
50. Albright, F., Smith, H. P., and Richardson, A. M. Post-menopausal osteoporosis: its clinical features. *J. A. M. A.* **116**:2465-2474, 1941.
51. Adams, M., Boothby, W., and Snell, A. Metabolic studies in osteoporosis. *Am. J. Physiol.* **114**:383-398, 1936.
52. Carlson, H. E., and Ockerblad, N. F. Stones of recumbency. *South. M. J.* **33**:582-593, 1940.
53. Barney, J. D., and Jones, G. E. Some problems in the management of urinary calculi. *J. Urol.* **45**:1-12, 1941.
54. Kempster, E., Breiter, H., Mills, R., McKey, B., Bernds, M., and Outhouse, J. The utilization of the calcium of dicalcium phosphate by children. *J. Nutrition* **20**:279-287, 1940.
55. Horn, W. S. Geriatrics as a modern specialty. *Texas State J. Med.* **33**:448-453, 1937.
56. Editorial: Unit on gerontology in the National Institute of Health. *U. S. Pub. Health Rep.* **55**:2099-2101, 1940.
57. Cowdry, E. V. *Problems of Ageing: Biological and medical aspects.* 758 pp. Baltimore: Williams & Wilkins Co., 1939.
58. Sherman, H. C. The bearing of the results of recent studies in nutrition on health and on length of life. *Bull. New York Acad. Med.* **13**:311-323, 1937.
59. Langstroth, L. Relation of American dietary to degenerative disease. *J. A. M. A.* **93**:1607-1613, 1929.
60. Harris, S.: in discussion of Tuohy.[67]
61. Meyer, J. The management of diseases of the gastro-intestinal tract in the aged. *M. Clin. North America* **24**:9-21, 1940.

62. Jeghers, H.: unpublished data.
63. Meyer, J., Golden, J. S., Steiner, N., and Necheles, H. The ptyalin content of human saliva in old age. *Am. J. Physiol.* 119:600-602, 1937.
64. Meyer, J., Spier, E., and Neuwelt, F. Basal secretion of digestive enzymes in old age. *Arch. Int. Med.* 65:171-177, 1940.
65. Meyer, J., and Necheles, H. Studies in old age: the clinical significance of salivary, gastric and pancreatic secretion in the aged. *J. A. M. A.* 115:2050-2053, 1940.
66. Cowdry.[57] P. 206.
67. Tuohy, E. L. Geriatrics in relation to an adequate energy producing and protective diet. *J. A. M. A.* 114:223-227, 1940.
68. Editorial: Geriatrics: the care of the aged. *J. A. M. A.* 109:2143, 1937.
69. Robertson, J. D. Calcium and phosphorus studies in normal people: including old age. *Lancet* 2:97-100, 1941.
70. Dunlop, H. Diet in old age. *Practitioner* 139:46-54, 1937.
71. Cleckley, H. M., Sydenstricker, V. P., and Geeslin, L. E. Nicotinic acid in the treatment of atypical psychotic states associated with malnutrition. *J. A. M. A.* 112:2107-2110, 1939.
72. Piersol, G. M., and Bortz, E. Le R. The aging process: a medical-social problem. *Ann. Int. Med.* 12:964-977, 1939.
73. Horn, W. S. Diet in old age. *M. Press* 203:152-154, 1940.
74. Tuohy, E. L. A proper and adequate protein diet for elderly people. *Minnesota Med.* 23:313-317, 1940.
75. *Idem*: An adequate dietary in later life. *Wisconsin M. J.* 39:353-360, 1940.
76. Barowsky, H. A method of nutritional protection during senescence. *M. Rec.* 152:149, 1940.
77. Bourne, G. *Nutrition and the War.* 126 pp. Cambridge: University Press, 1940.
78. Booher, L. E. Adequate nutrition for the industrial worker. *J. A. M. A.* 114:548-553, 1940.
79. Orr, J. The nation's larder in wartime: national food requirements. *Brit. M. J.* 1:1027-1029, 1940.
80. Drazin, M. L. Nutrition and national defense. *Mil. Surgeon* 88:39-50, 1941.
81. Underwood, E. J. The significance of the "trace elements" in nutrition. *Nutrition Abstr. & Rev.* 9:515-534, 1940.
82. Shohl, A. T. *Mineral Metabolism.* 384 pp. New York: Reinhold Publishing Co., 1939. P. 234.
83. Daniel, E. P. Trace elements. In *Food and Life.*[23] Pp. 213-220.
84. Aughey, E., and Daniel, E. P. Effect of cooking upon the thiamin content of foods. *J. Nutrition* 19:285-296, 1940.
85. Rose, M. S. The effect of quick freezing on the nutritive value of foods. *J. A. M. A.* 114:1356-1361, 1940.
86. Horvath, A. A. The nutritional value of soybeans. *Am. J. Digest. Dis.* 5:177-183, 1938.
87. Editorial: The soya bean in dietetics. *Brit. M. J.* 1:982, 1940.
88. Bourne.[77] P. 48.
89. Jokl, E., and Cluver, E. H. Physical fitness. *J. A. M. A.* 116:2383-2389, 1941.
90. Olmsted, W. H. The diet of the doctor. *J. Kansas M. Soc.* 42:1-5, 1941.
91. Sinclair, R. G. The nutritional significance of fat. *Canad. M. A. J.* 38:491, 1938.
92. Wilder, R. M. Nutrition planning for the national defense. *War Med.* 1:143-157, 1941.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 27441

PRESENTATION OF CASE

A sixty-two-year-old railway-express agent was admitted to the hospital because of ascites of at least nine years' duration and because of fever dating from the appearance of swollen lymph nodes in his neck eight weeks prior to admission.

His illness apparently began nine years before entry, when, following the passage of black stools for two or three days, he had a severe hematemesis. He then entered a hospital, and was found to have ascites. He was tapped twice; each time about 14 quarts of fluid was withdrawn. A duodenal ulcer was said to have been demonstrated by x-ray study. The patient remained quite ill for seven months, but was then in good health until three years before admission. He then experienced another hematemesis, and entered another hospital, where duodenal ulcer was again said to have been demonstrated by x-ray examination. Two years later, in addition to a "cold," he developed a rash resembling hives all over his body. Following nausea, he had a severe hematemesis, for which he was again taken to the other hospital. He remained there five weeks, and was again told that x-ray films showed an ulcer.

Eight weeks before entry, lymph nodes on the left side of the neck (which had been lanced twice during the previous nine years) became swollen, and the temperature rose to 104°F. The lymph nodes were incised and drained. Following this episode, there was daily elevation of temperature, weakness and fatigue.

The family history was irrelevant.

The patient had had a transient attack of jaundice twenty-five years before entry but had been quite well thereafter. He denied the taking of alcohol. His appendix had been removed thirty-five years before entry.

Examination showed a man with a tremendous abdomen, accentuated by thinness of the extremities and a meagerness of subcutaneous fat. There was shifting dullness in the abdomen, and the liver seemed small. One observer thought that the spleen was palpable. An old appendectomy scar was present. The superficial veins of the abdomen were dilated, and there were many hemorrhoids. The skin was dry, warm and slightly icteric; the scleras were similarly jaundiced. A draining sinus, approximately 7 cm. in length, lay in the left lower lateral cervical region. There was diminished expansion of the lungs, with a few rales at the right base posteriorly. The heart was not enlarged. The blood pressure was 110 systolic, 50 diastolic.

The temperature was 104°F., the pulse 120, and the respirations 32.

Examination of the blood showed a white-cell count of 8000, with 88 per cent polymorphonuclears. The red-cell count was 3,600,000, with 9 gm. hemoglobin. The urine showed a + test for albumin and contained red and white cells. The stools gave ++++ guaiac reactions on nine out of ten examinations. The van den Bergh reaction was biphasic, with 3.8 mg. per 100 cc. The blood nonprotein nitrogen was 19 mg. per 100 cc. Agglutination tests for typhoid fever and brucellosis were negative.

Paracentesis was performed, and about 9 liters of greenish-yellow fluid, which was sterile on culture, was removed. The specific gravity of the fluid was 1.010. Abdominal taps on the fifth and eighteenth days yielded respectively 4 and 5 liters of similar fluid.

The pus from the sinus in the neck grew a few colonies of *Staphylococcus aureus*. A blood culture taken on the twelfth hospital day was negative.

A roentgenogram of the chest showed incomplete aeration of the lower lobes, especially the right. Free air lay beneath the right diaphragm. Shortly after the fourth paracentesis, the patient was given an injection of Thorotrast. Subsequently, a roentgenogram showed very little increase in density of the liver. The spleen was somewhat denser, and appeared considerably enlarged. The film also showed some irregularity of the inferior margin of the glenoid fossa of the left scapula, which was not entirely characteristic of a metastatic lesion.

While the patient was in the hospital, the temperature fluctuated daily from 100 to 103°F. On the twenty-third hospital day, there was a sudden drop in temperature to 95°F. following a hematemesis. The blood pressure fell to 110 systolic, 60 diastolic, and the pulse became slow and thready. The patient rallied for a few days, but lapsed into coma and died on the twenty-eighth day.

DIFFERENTIAL DIAGNOSIS

DR. WALTER BAUER: Am I to believe that the patient had ascites for nine years?

DR. TRACY B. MALLORY: He had it nine years before entry and again on entry; that is the extent of our information.

DR. BAUER: Do you know anything about the initial illness? Did he have fever or jaundice, and why was he kept in the hospital so long?

DR. MALLORY: I cannot answer the questions.

DR. BAUER: The rash resembling hives is of no diagnostic help to me. Did this man ever have any symptoms suggesting duodenal ulcer?

DR. MALLORY: I do not know.

DR. LOWREY F. DAVENPORT: The best story came from the outside doctor, who followed the case for fifteen years and was convinced that the bleeding nine years before entry was quite typical of ulcer; x-ray examination in several places confirmed the diagnosis. The patient had had a protuberant abdomen for years, and because of this we had a great deal of difficulty persuading him to come to the hospital. He said that his abdomen had always been large, and not until we showed him that his trousers lacked 10 inches of meeting was he convinced that he was unusually large.

DR. BAUER: He had a swollen abdomen. We do not know how much significance to attach to the abdominal findings, because determining the size of the liver and spleen under these conditions is always difficult.

Patients with cirrhosis may require innumerable paracenteses over a period of years. It is possible to have ascites due to portal obstruction for a period of nine years. On the other hand, unless the history is very inadequate, the patient was extremely well between the episodes of gastrointestinal bleeding; I should therefore be inclined to believe that there were times when he had little or no ascites.

The chest signs, I presume, were consequent to the large amount of ascitic fluid.

The temperature of 104°F. is probably of significance, particularly in that we are dealing with a man who had what would seem best interpreted as portal obstruction. He obviously had suffered from gastrointestinal bleeding from time to time, and this was the reason for his seeking hospital admission. That he was jaundiced is shown by the van den Bergh reaction.

The ascitic fluid, from the information given, seems to have been a transudate rather than an exudate. Was it by any chance injected into a guinea pig?

DR. MALLORY: No.

DR. BAUER: A roentgenogram subsequent to the injection of Thorotrast showed very little increase in density of the liver. This finding would be in keeping with the diagnosis of chronic liver disease, such as cirrhosis, because Thorotrast is taken up by the reticuloendothelial system. If the liver is diseased, one expects a reduction in that system and, consequently, no increase in density of the liver, following the injection of this substance.

Have we the x-ray films here? Is there any suggestion of pulmonary disease? Is there any reason to believe that the patient had tuberculosis?

DR. JAMES R. LINGLEY: The lungs are clear, except for this atelectasis at the base, as described. The diaphragm is high on both sides, probably because of ascites, and this leads to some compression atelectasis at the bases, more marked on the right. The lungs are otherwise clear. The aorta is quite tortuous. This is the area referred to in the inferior margin of the glenoid fossa, about which I cannot help you very much. The changes are very indefinite. The first thing I should think of is Paget's disease, but it could be metastasis.

DR. BAUER: Is there any reason to suspect tuberculosis?

DR. LINGLEY: No; this is the abdominal film, showing the spleen enlarged and increased in density by Thorotrast. The liver, on the other hand, is much less dense than the spleen. It should be denser after Thorotrast. It does not appear to be enlarged.

DR. BAUER: You do not think this could be an end result of septic arthritis some years previously?

DR. LINGLEY: The changes are too localized, and there is no narrowing of the joint spaces.

DR. BAUER: Do you think that the bone is denser here than here?

DR. LINGLEY: It looks a little irregular and increased in density along the margin. I should put Paget's disease first.

DR. BAUER: I should think there was little doubt that we are dealing with a man who had physical findings consistent with portal obstruction due to cirrhosis of the liver. In addition, he had a suppurative, cervical adenitis. The very fact that the latter had been present on two occasions previously and had been incised some eight weeks before and was still draining leads me to believe that this man had, in addition to a portal obstruction, tuberculous adenitis. We have from the history good reason to think that he had evidence of portal obstruction in the initial illness nine years previously. I further believe that he had sufficient improvement in liver function to be able to carry on fairly normally for some time thereafter. The fact that he did not use alcohol

was in his favor, and may have been responsible for his having lived so long. There are a number of questions to which we should like to know the answers. What was the cause of the repeated hematemeses? The patient had been x-rayed on three occasions in two or three different institutions, and each time he was reported to have a duodenal ulcer. On the other hand, according to my interpretation, he was suffering from a disease that is sometimes complicated by hematemesis, namely, portal cirrhosis of the liver. He had three massive hemorrhages and lived nine years. If the bleeding was from esophageal varices, it is very unusual, but I suppose it could and I believe it does happen; therefore, bleeding alone does not enable us to state whether these hematemeses always resulted from a duodenal ulcer or varices or perhaps both. I am a little inclined to believe, although I am unable to prove it, that the final hematemesis could very well have been due to bleeding from eosphageal varices. If we are dealing with a man who had evidence of portal obstruction due to cirrhosis for at least nine years, esophageal varices would not be unusual. I take it that no gastrointestinal examinations were made here.

DR. MALLORY: None were made in this hospital.

DR. BAUER: If varices were looked for, they were not found, or at least they were not mentioned in any of the x-ray reports. I rather hesitate to throw out the diagnosis of duodenal ulcer.

What was the cause of the fever? A suppurative adenitis is sufficient cause for a temperature of 104°F. However, patients with cirrhosis may run a low-grade fever. The combination of the suppurative adenitis and cirrhosis of the liver would adequately account for the fever. The intercurrent infection probably served as a sufficient additional load on the liver to precipitate serious liver failure. One might explain the fever on the basis of such a combination of factors. The very fact that this man had cirrhosis for at least nine years means that we must bear in mind the possibility of a hepatoma, which may also cause fever.

There remains still another possibility, namely, tuberculous peritonitis, a complication of cirrhosis of the liver. I have interpreted the cervical adenopathy as being tuberculous in nature and therefore wonder if a hematogenous spread had not resulted in tuberculous peritonitis. If this occurred, we must also raise the possibility of miliary tuberculosis. The cause of death was obviously hematemesis in a man who was seriously ill at the time he entered the hospital. As I said before, I believe that the final hematemesis was due to bleeding from esophageal varices.

We might reconstruct this story as follows: catarrhal jaundice twenty-five years previously, followed by cirrhosis of the liver, an occasional sequela. Subsequently, an exacerbation of the tuberculous adenitis, with eventual dissemination of tubercle bacilli, resulted in tuberculous peritonitis and perhaps tuberculosis elsewhere. This added infection was responsible for further injury to the liver. The last hematemesis was responsible for his exitus. I realize that a diagnosis of tuberculous adenitis and cirrhosis of the liver, in addition to hemorrhage from either a duodenal ulcer or an esophageal varix, is adequate to account for all that this man showed, but I am rather intrigued with this other possibility, because we know that tuberculous peritonitis is one of the complications of cirrhosis of the liver.

For my final diagnosis, I shall say that this man at autopsy showed cirrhosis of the liver, tuberculous adenitis, tuberculous peritonitis, healed duodenal ulcer, possibly miliary tuberculosis and possibly hepatoma, and that he died of ruptured esophageal varices. The x-ray changes in the glenoid fossa are left unaccounted for. If my memory serves me correctly, metastases from hepatoma are not very common, especially this far removed.

DR. MALLORY: Hepatoma does metastasize to bone.

DR. BAUER: Yes; but it is not very common. This picture is consistent with Paget's disease, and I should like to account for the bone lesions on this basis. This would make my interpretation much easier.

DR. J. H. MEANS: I should like to cite a case with several points of similarity that bear on the combination of cirrhosis of the liver and hematemesis. Several years ago, there was a man, older than this one, who the service thought had the classic picture of cirrhosis of the liver, with ascites, hematemesis and so forth. We thought, of course, that he was bleeding from varices but the X-ray Department persistently refused or were unable to find any varices, which was a little disconcerting. The patient died, and it was proved that he did not have cirrhosis of the liver or varices and bled from a duodenal ulcer.

DR. BAUER: I do not see how one can say that this mistake did not occur in this case. I realize that it is rather foolish of me to assume that the hemorrhage came from esophageal varices. After all, three hospitals have stated that he had a duodenal ulcer, and it is hard to go against these reports. On the other hand, a man who has had

cirrhosis of the liver for nine years is an excellent candidate for esophageal varices.

DR. WYMAN RICHARDSON: What about the specific gravity of the abdominal fluid? It was 1.010. Would that be evidence against tuberculous peritonitis?

DR. BAUER: I think it would. On the other hand, marked ascites and slight exudation might give such a figure. That would not disturb me unduly.

DR. MALLORY: A point raised by Dr. Chester M. Jones was that the patient had just had a large hematemesis. Ascites frequently occurs after hemorrhage as the result of a sudden lowering of the serum protein. Such a mechanism might affect the specific gravity of the fluid.

CLINICAL DIAGNOSES

Abscesses of liver, multiple.
Cirrhosis of liver, toxic.

DR. BAUER'S DIAGNOSES

Cirrhosis of liver.
Tuberculous adenitis.
Tuberculous peritonitis.
Duodenal ulcer, healed.
Miliary tuberculosis?
Hepatoma?
Ruptured esophageal varices.

ANATOMICAL DIAGNOSES

Liver abscesses, multiple.
Tuberculous cervical adenitis and peritonitis.
Miliary tuberculosis, generalized.
Cholecystitis, chronic.
Cholelithiasis.
Choledocholithiasis.
Esophageal varices (no thrombosis of portal and splenic veins).
Ascites.

PATHOLOGICAL DISCUSSION

DR. MALLORY: Several of Dr. Bauer's predictions are correct, but the bases on which he founded his reasoning are almost entirely incorrect as judged from the results of autopsy. The patient had a generalized tuberculosis, with frankly caseous cervical lymph nodes, with an extremely extensive tuberculous peritonitis and with miliary tubercles throughout the spleen and liver. There was no cirrhosis. There was no mechanical portal obstruction. I did not believe the intern, and I personally dissected out the portal vein. There were esophageal varices, unexplained, and no trace of any ulcer in the duodenum or any scars. There were two very large liver abscesses, one 3 and one 5 cm. in diameter. There were stones in the gall bladder and the common duct, and there was a cholangitis. I believe that the liver abscesses were pyogenic in character. On smear, the pus contained many diphtheroid bacilli; no tubercle bacilli were found. The explanation for the varices in the absence of portal obstruction, I cannot offer. I have seen it four or five times, and it does occur.

One can only guess, it seems to me, in retrospect about the ascites nine years before entry. Tuberculous peritonitis at that time with spontaneous recovery is the best guess. One certainly does see spontaneous recovery from tuberculous peritonitis, and I cannot believe that he could have had a portal obstruction that left no trace.

DR. WILLIAM B. BREED: What was the size of the liver and spleen?

DR. MALLORY: The spleen weighed 600 gm.; the liver was normal in size, weighing 1500 gm.

A PHYSICIAN: What were the other cases of varices and no portal obstruction?

DR. MALLORY: They occurred chiefly in elderly men. I remember only one specifically, a man in the late seventies or early eighties, with massive hematemesis from esophageal varices but no portal obstruction.

DR. BAUER: Do you conclude that he did not have duodenal ulcer and that he had always bled from varices?

DR. MALLORY: It is the only conclusion I can reach.

DR. RICHARD H. SWEET: What did the clinicians have in mind when they gave Thorotrast — liver abscess?

DR. MALLORY: It sounds as if they did.

DR. DAVENPORT: It was given at the suggestion of Dr. Jones, who believed that the prognosis was hopeless, and that there was no danger in giving it. He hoped to outline an abscess or hepatoma.

A PHYSICIAN: What was the clinical diagnosis?

DR. DAVENPORT: Cirrhosis of the liver, with presumable liver abscess because of the fever. The lymph nodes we considered tuberculous — I do not believe we laid enough emphasis on the possibility of tuberculous peritonitis.

CASE 27442

PRESENTATION OF CASE

A forty-three-year-old Negro stableman was admitted to the hospital because of severe pain in his chest for about twelve hours.

The patient had been well until about three months before entry, when he developed a cough that was productive of blood-stained sputum. The

cough was painless, and was always more severe at night, after he had gone to bed. After a month, the sputum ceased to be blood tinged, and remained yellow and purulent.

The patient was free from other symptoms until the night before entry, when, while sitting in front of his barn, he was attacked quite suddenly by pain in the left side of his chest. The pain was sharp, severe, and so aggravated by breathing that he dared scarcely to inhale. He took some whiskey to ease the pain, and went to bed. He slept for a while, only to awake with a similar pain in the right chest. Later in the night, he sweated profusely and had a frank, shaking chill. The next morning, he entered the hospital in considerable distress, complaining of pain on both sides of the chest.

While the patient was a child, both his parents had died of tuberculosis. He had followed race horses all his life, living in or near stables. Twenty years before entry, he had received a large knife wound in the right upper arm. Syphilis was denied, but he had received arm and hip "shots" for a "cold" the winter before entry.

In the three months preceding admission, he had lost 15 pounds.

On examination the patient appeared well developed and well nourished despite some recent weight loss. The expansion of his chest was limited bilaterally. There was occasional coughing, brassy in character. Loud friction rubs were heard over the lower half of each lung field. Breath sounds were definitely diminished in the left chest, although tactile and vocal fremitus were normal, and there were no changes to percussion. The heart did not seem enlarged. The blood pressure was 140 systolic, 90 diastolic.

The temperature was 101°F., the pulse 104, and the respirations 28.

The blood showed a red-cell count of 3,190,000, with 11 gm. hemoglobin. The white-cell count was 14,750 per cu. mm., with 85 per cent polymorphonuclears. The blood Hinton and Wassermann reactions were both positive. Repeated blood cultures were negative. The urine was not remarkable. Numerous examinations of the sputum failed to reveal tubercle bacilli or fungi. On one occasion, a Type 3 pneumococcus was isolated.

A roentgenogram of the chest showed slight enlargement of the heart, affecting especially the left ventricle. At the junction of the ascending portion and arch of the aorta, there was a multilobular dilatation, which seemed to compress slightly the left main bronchus. There was mottled consolidation in the left lower lobe of the lung, in the lower half of the right upper lobe and in the right lower lobe. The left upper lobe seemed emphysematous. There was no free pleural fluid. The patient was given sulfathiazole and later switched to sulfapyridine. The temperature continued to fluctuate daily from 99 to 102 or 103°F., but the pain disappeared and the cough improved. Early in the fourth week of his hospital stay, severe pleuritic pain in the left chest reappeared for a few days. Re-examination showed dullness in the left axilla and at the left base, with diminished breath sounds. A patch of tubular breathing was present at the left base anteriorly. After this, the patient was given potassium iodide in daily doses, and weekly injections of bismuth.

Another roentgenogram of the chest, taken a month after the earlier film, showed several cavities in the left lower lobe, with fluid levels. The area of infraclavicular consolidation had increased and seemed to include a small cavity.

Bronchoscopy was performed late in the sixth hospital week. The left main bronchus was narrowed and edematous at the orifice, with a considerable amount of thick, gelatinous mucoid secretion. The bronchus to the left lower lobe was narrowed, and contained similar mucoid secretion. A biopsy of the mucosa of the left main bronchus showed no diagnostic abnormality. A roentgenogram of the skull showed no evidence of intracranial metastatic lesions.

On the fifty-ninth hospital day, without premonition, the patient suddenly had a massive hemoptysis, spraying blood all over the room. His mouth and nose filled with frothy clot, and he became pulseless and expired.

Differential Diagnosis

Dr. Edward F. Bland: This was a dramatically fatal illness, so far as I can judge from the record, extending over a period of only five months. In exploring the various possibilities, I think we must keep in mind what to me seem to be the essential features of this illness, namely, a progressive subacute pneumonic process in both lungs leading to abscess formation, cavitation and terminal erosion of a large arterial vessel. The diagnostic problem concerns the specific etiologic agent involved, and I hope for considerable help from the X-ray Department on this point. There are two specific questions I should like to ask the roentgenologist. I am bothered by the term "multilobular dilatation" of the aorta. I should like to clear that point up, because most syphilitic alterations in the aorta result in either a diffuse dilatation or a saccular aneurysm. Secondly, does Dr. Lingley find any evidence in the films to indicate osteomyelitis of the thoracic cage?

Dr. James R. Lingley: There are a number of films, taken over an interval of five weeks. The first film shows widening of the superior mediastinum, which was due to enlargement of the aorta. In the lateral view, one can see marked anterior bulging of the ascending portion and also dilatation of the upper part of the descending portion of the aorta, producing much compression and narrowing of the left main bronchus. The ascending aorta is definitely dilated in a fusiform manner and also shows localized bulges—hence the term "multilobular dilatation." The lesion in the descending aorta is a saccular aneurysm. The process in the lungs at the first observation consisted of a bilateral mottling most evident on the left side at the base and on the right in the midchest and upper chest. During the period of observation, this changed considerably. The process at the left base increased markedly over a period of five days, while the process in the right upper diminished. The patient then developed a new process in the left upper lung, followed at a later period by cavity formation both here and in the area of consolidation at the left base. The thoracic cage appears normal.

Dr. Bland: Now that I have seen the films, I am willing to accept the x-ray interpretation of multiple aneurysmal dilatations of the aorta. Of more importance are the pulmonary lesions. We are dealing with a Negro, and the first thing that comes to my mind is "galloping consumption." There is, however, some very good bacteriologic evidence against it, so much so that I doubt if this patient actually had tuberculosis. In the first place, with an acid-fast bronchopneumonic process of this extent, it is usually relatively easy to demonstrate bacilli in the sputum. I am sure that a very thorough search was made for these organisms, and I am reasonably certain, since this man was on the ward here, that the study included repeated examinations of the gastric contents.

Dr. Tracy B. Mallory: It did.

Dr. Bland: Furthermore, it is probably true that the material was not only examined but also injected into suitable animals.

Dr. Mallory: Guinea-pig inoculation was done, but no report was available at the time of the patient's death.

Dr. Bland: Nevertheless, I think the strongest bit of evidence, and in fact the only evidence, against tuberculosis is that the organism in this very active process was not demonstrated. Secondly, the lesions here are predominantly at the base of the lungs; that is somewhat against tuberculosis. Finally, I think there are two clues in the clinical record indicating that those in charge of the patient discarded the idea of tuberculosis: they treated him with iodides—consequently, they must have had some other etiologic factor in mind at that point; also, the patient was bronchoscoped. Ordinarily, in the presence of an active tuberculous process, one does not administer iodides nor does one like to bronchoscope the patient, unless there are very special indications for the latter procedure. Adding up this evidence, then, I shall have to discard tuberculosis.

Next, in searching for other possibilities, I am rather impressed by the fact that three times in the record we are told that this man was closely associated with horses and stables. The Pathology Department in these exercises does not usually stress such possible clues so persistently; therefore, I suppose I should pay special attention to them. Following this lead, the first thing to think of is mycotic infection of the lung. By that term, one means a variety of infections in the lung due to fungi, molds and yeasts. The commonest fungous infection among people who deal with animals and stables is actinomycosis. When the lung is involved, there are often lesions of the skin or subcutaneous structures, not infrequently resulting in draining sinuses. We have no evidence of such lesions here, and Dr. Lingley has pointed out that there was no rib involvement. On the other hand, approximately 15 per cent of actinomycosis in human beings may be limited to the lungs. In others, it may be limited to the gastrointestinal tract. It is of some interest that most people believe infection takes place not by direct contact with infected animals or by eating the meat of such animals, but rather from the handling of hay and grain. I hope Dr. King will correct me if I have made any misstatements in this connection, for I naturally do not feel so much at ease in dealing with the lungs as with the heart. In considering actinomycosis as possibly responsible, I am a little bothered that the ribs were uninvolved, and that there were no draining sinuses. I am also further disturbed by the fact that they were not able to demonstrate the organism either in the sputum or in the material that came from the bronchoscopic examination, but this does not exclude actinomycosis. On the other hand, the somewhat chronic course with hemoptysis and cavity formation is a part of the general clinical picture of mycotic infection of the lung, especially actinomycosis. The mucoid character of the sputum is fairly characteristic. Another point somewhat against it is that the patient presumably did not respond to chemotherapy. However, I do not believe we have had enough experience with chemotherapy in mycotic infections to assess this

evidence one way or the other. There are several reports pointing out that some patients do respond favorably. We also do not know how much chemotherapy was actually given. Perhaps there was some special reason for switching from sulfathiazole to sulfapyridine and then omitting it entirely. Perhaps they were never able to get the blood level high enough, but we can only speculate about that. I must say that since acid-fast bacilli could not be found I view with favor the possibility of actinomycosis.

In searching for other possibilities in a person associated with stables, one thinks of tetanus. There is no place here for tetanus that I can see. Then we think of anthrax. There are reported cases of pulmonary anthrax, a rapidly fatal disease; the patient usually dies in a few hours or a day or two and actually often before physical signs are demonstrable in the lungs. Finally, there is the possibility of glanders in the lung; but that would be a little fanciful here.

Another condition one must think of as a cause of subacute or chronic pulmonary consolidation is Friedländer's pneumonia. About 3 per cent of pneumonias are due to the gram-negative encapsulated Friedländer's bacillus. It is usually acute, lasting something like eight to fourteen days; but now and then it may be a more chronic process such as this patient showed, and it is often associated with hemoptysis, consolidation and multiple cavitation of the lung — the result of a non-putrid pulmonary necrosis. The sputum is often mucoid, but I am also disturbed here by the fact that the organism could not be demonstrated. There is no specific statement in the record concerning Friedländer's bacillus; it would have been mentioned if found. Therefore, I think that this was not Friedländer's pneumonia.

Is there any possibility of neoplastic disease, either primary or secondary, carcinoma or lymphoma? I do not believe so. The x-ray report does not suggest it. The bronchoscopic examination simply shows narrowing of the left main bronchus, probably from external pressure of the dilated aorta, possibly in part from chronic inflammatory swelling inside the air passage itself. Biopsy of this area failed to reveal evidence of cancer.

We know that the patient had syphilis. Can we bring syphilis into the picture otherwise than by its probable involvement of the aorta? Syphilis of the lung itself is rare. Cases of gumma have been described, and have been seen here in this hospital. This patient was treated with iodides and bismuth, not, I suppose, because anyone thought there was syphilitic involvement of the lung but rather because the patient had positive serologic findings and a large aorta. Rarely, syphilis may involve the pulmonary artery, usually with aneurysmal dilatation, or very occasionally as a form of endarteritis of the smaller radicles; but I see no evidence for suspecting such a diagnosis here.

Did the patient inhale a foreign body that caused obstruction, secondary infection and bronchiectasis? There is no evidence to suggest it from the history or subsequent course.

I keep asking myself whether we are trying to make this case too complicated. Was this, after all, simply bronchiectasis of the lung present for a long time and more or less latent until the terminal infection? There were no symptoms in the past to suggest such a process. They are not always necessary. Perhaps bronchiectasis from pressure by the aneurysm on the left main bronchus, with secondary infection behind it that later spread to the other lung, is a possibility. I do not see how we can say yes or no. I am inclined to think that there was some specific infectious disease of this lung other than simple mechanical obstruction of the bronchus and trapped infection.

After exploring these various etiologic possibilities, I can briefly summarize by saying that I am back to where I started. The evident diagnosis is that of a bilateral pulmonary infection with multiple abscess formation and cavitation of undetermined etiology, in addition to a question of actinomycosis. The patient undoubtedly had syphilis, with aneurysmal dilatation of the aorta. Then there was the terminal pulmonary hemorrhage. Obviously, a large vessel was eroded. Was it the aorta? Was it rupture from pressure within, was it aggravated by weakening of the wall of the vessel from without, or was it simply an erosion of a large pulmonary vessel? I do not see how we can decide. My impression is that rupture of the aorta leads to rather instantaneous death. In this case, those who saw the patient had time to make a few observations. They did not say whether the blood was bright red or dark red, suggesting it might have been from the aorta in the first event or from the pulmonary artery in the second. I do not know how we can decide where it came from, but certainly it was from a large arterial vessel.

Dr. Donald S. King: We saw this patient several times in the Thoracic Clinic. At first, we agreed with the student who took the history that the diagnosis was pulmonary tuberculosis, but we were baffled by the repeated negative sputum examinations, and began to look for other possible etiologic factors. Because of his association with horses, we thought, as Dr. Bland did, of actino-

mycosis, but could never prove it. In speaking of actinomycosis, it might be well to note that the disease may develop in city dwellers who have had no contact with animals. We recently had such a case in a young female stenographer. In the present case, we thought also of Friedländer's infection, but could not find the organism. We then got interested in the possibility of pulmonary syphilis and agreed with the recommendation that antisyphilitic treatment be tried.

Dr. Bland raised the question of bronchoscopy in cases of pulmonary tuberculosis, and I should perhaps say that, at times, even with acute pulmonary tuberculosis, bronchoscopy is indicated. We are coming to recognize bronchial tuberculosis as a fairly common complication. An acute bronchial obstruction from tuberculous infection may have to be relieved by the bronchoscopic procedure. If proper drainage can be established, fever and other untoward symptoms may be promptly relieved. In the present case, if there was definite evidence of obstruction to the left lower-lobe bronchus, bronchoscopy was justified, even though there was the possibility of the diagnosis of tuberculosis.

Dr. Lingley, if you saw this x-ray film and did not know the story, would the diagnosis be evident?

Dr. Lingley: The x-ray appearance would fit actinomycosis very well, in spite of the lack of rib destruction. It is unusual for tuberculosis to be at the base predominantly and for the consolidation to fluctuate so much. I do not know of any positive method of making a diagnosis of syphilis of the lung, although various criteria have been suggested. I think actinomycosis is as good as anything.

Dr. King: Would you have guessed that if you had seen the film?

Dr. Lingley: Chronic pulmonary infection with cavitation is as far as I can go on the films alone.

Dr. King: I know the diagnosis now, but as I see the films from here it seems that we should have made the diagnosis from them. The fact that the process was predominantly basal does not rule out tuberculosis. There also was bilateral apical infection.

Dr. Bland: What was the clinical diagnosis on the death report?

Dr. Mallory: Chronic pulmonary suppuration, tertiary syphilis, with aortic aneurysm and terminal rupture into a bronchus.

Dr. Bland: Where did you think the terminal hemorrhage came from?

Dr. King: I know the autopsy findings, but I think that the service made the correct diagnosis.

Clinical Diagnoses

Chronic pulmonary suppuration.
Tertiary syphilis, with aortic aneurysm and terminal rupture into a bronchus.

Dr. Bland's Diagnoses

Chronic pulmonary infection of undetermined etiology (actinomycosis?)
Multiple pulmonary abscesses.
Tertiary syphilis.
Aortic aneurysms.
Terminal hemorrhage.

Anatomical Diagnoses

Syphilitic aortic aneurysms (three), with rupture of one into the left lower bronchus.
Hemorrhage into lung.
Syphilitic aortitis.
Compression of left bronchus by aortic aneurysm.
Pulmonary tuberculosis, bilateral, with cavitation.
Secondary erosion of vertebral bodies by aneurysmal dilatations.

Pathological Discussion

Dr. Mallory: The autopsy showed marked dilatation of the aorta, with multiple aneurysms, two of which were definitely saccular, the third being a more diffuse dilatation. The larger aneurysms were found in the ascending portion, and the smallest aneurysm was just beyond the arch in the descending portion. It had become adherent to the left primary bronchus and had ruptured into it terminally; death was due to the inhalation of tremendous amounts of blood throughout the bronchial tree and even into some of the alveoli. The patient essentially drowned in his own blood rather than dying of hemorrhage. The pulmonary picture was somewhat confused from the gross point of view by the massive inspiration of blood, but many areas of consolidation were found scattered throughout all lobes of the lung, some of which showed varying degrees of caseous softening and some frank cavitation. On gross examination, it was not recognized as tuberculosis, but on microscopic examination it was perfectly obvious. Eventually, the guinea pig that had been inoculated with the gastric contents was found to show tuberculosis. The heart itself was not involved in the aortic process. The lesion was too high to affect either the aortic valve or the coronary ostia.

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The Journal does not hold itself responsible for statements made by any contributor.

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AMERICAN COLLEGE OF SURGEONS

From November 3 through November 7, the surgeons of Metropolitan Boston will be hosts to the clinical congress of the American College of Surgeons, with headquarters at the Hotel Statler. These annual meetings are among the greatest and most effective educational gatherings that are held by any branch of the profession. The surgeons of the large local hospitals will demonstrate their methods and ability, and many distinguished visitors will give addresses or take part in the discussions. Among the guest speakers will be Dr. Evarts A. Graham, of St. Louis, the president of the college, and Dr. W. Edward Gallie, of Toronto, the president-elect. From abroad will come Rear-Admiral Gordon Gordon-Taylor, of London, and Professors Pablo Luis Mirizzi, of Cordoba, Argentina, and Moacyr Eyck Alvaro, of Sao Paulo, Brazil.

In addition to surgical clinics, round-table conferences and scientific meetings in the daytime, the Presidential Meeting and Convocation is scheduled for Monday evening, and formal scientific lectures for the following three evenings. On Friday evening, the Boston Surgical Society will hold a special meeting, at which Dr. Allen O. Whipple, of New York City, will be awarded the Bigelow Medal.

Matters pertaining to hospital standardization will be discussed at meetings held at the Copley-Plaza. These gatherings should be of interest to physicians, hospital executives, nurses and laymen, and particular emphasis will be placed on proper systems for the making-out and filing of hospital records.

Admission to the clinics and surgical round-table conferences will be by ticket only, to prevent overcrowding. For members or junior candidates of the College, the registration fee is $5.00, payable at the registration desk at the Hotel Statler; candidates accepted by the College for induction at this meeting may register without charge. For nonfellows attending the congress as invited guests of the College, the registration fee is $10.00. No fee is involved for attendance at the meetings concerned with hospital standardization, but all who plan to be present should register at the desk at the Copley-Plaza.

NUTRITION AND DEFENSE

The old adage, "An army travels on its stomach," might well be changed to "A nation travels on its stomach." There was a time when the fighting of wars did not greatly disturb the activities of much of the populace. But times have changed. World War II gives ample demonstration that efficiency and morale on the home front are as essential for winning wars as fighting on the battlefront. Warfare has so changed that millions of workers behind the lines are required for the continued delivery of supplies and mechanical equipment to the fighters. There is a

considerable medical literature to attest that malnutrition in its various forms impairs this physical efficiency and morale so essential to victory.

A recent study by Williams and Mason* adds convincing evidence for this contention. These investigators placed a number of healthy adults on a diet adequate in all respects but with a thiamin content of only 0.40 to 0.45 mg. daily. They point out that this approximates the thiamin content found by Stiebeling and Phipard in the diets of many American families. After four to six months, in addition to other manifestations, these subjects became depressed, irritable, quarrelsome, fearful, inefficient in work because of generalized fatigue, inattentive to details, uncertain of memory and lacking in manual dexterity. These symptoms slowly disappeared when additional thiamin was added to the diet. This is a convincing demonstration of the necessity of thiamin for emotional stability. Indeed, thiamin has been referred to in the lay press as the "morale vitamin," and people in the occupied countries are said to be more easily kept in a subjugated state because the low thiamin content of their diets has robbed them of their will to fight.

Thiamin, however, is only one of the many factors that may be absent in a poor diet. At the National Nutrition Conference for Defense, held in Washington this May at President Roosevelt's request, the frequent inadequacy of the American diet was frankly discussed. Specific recommendations for improving the nutrition of the people were made to the President. The exigencies of the hour necessitate that the advantages to accrue from the application of nutritional principles to defense efforts begin as soon as possible. Aside from these immediate objectives, the nutritional program now getting under way in this country has far-reaching implications and may materially influence the pattern of morbidity in the generations to come. At the conference, all physicians were urged to take an active interest in these nutritional problems and to assume leadership in the field. The progress report in this issue of the *Journal* reviews material with which every physician should be familiar.

*Williams, R. D., and Mason, H. L. Further observations on reduced thiamine (vitamin B_1) deficiency and thiamine requirement of man: preliminary report. *Proc. Staff Meet., Mayo Clin.* 16:433-438, 1941.

MEDICAL EPONYM

Krönig's Isthmus

Dr. Georg Krönig (1856–1911), docent in the University of Berlin, published his paper "Zur Topographie der Lungenspitzen und ihrer Percussion (On the Topography and Percussion of the Lung Apices)" in the *Berliner klinische Wochenschrift* (**26:** 809–812, 1889). A portion of the translation follows:

> The examination of a patient who had been referred to me was the beginning of a series of determinations of the borders of the lung apices, as well as the lung margins which I briefly report here. After I had determined the anterior supraclavicular margin of the lung in the usual fashion, that is by gentle percussion, I proceeded, still percussing very lightly to the posterior aspect and thereby obtained the following results. On the right side, as on the left, there appeared a line that extended medially in a wide arch, with its convexity directed inward, and approached to within a centimeter of the midline on the left at the level of a line between the second and third thoracic spines, on the right at the level of the fourth thoracic spine. In this case, the right apex was diseased . . . while the left showed a normal condition. . . . Inasmuch as I had obviously been successful in determining not only the height of the lung apices but also their breadth, . . . I tried to determine similarly the lateral margin. . . . The determination of the posterior lateral border is easy in many cases, especially in thin persons, but is frequently difficult in powerfully built, extremely muscular, or fat persons. The lateral border, which I have outlined on the anterior surface is extremely trustworthy. It runs from about the middle of the anterior margin of the trapezius muscle, curves down sharply, cuts the clavicle at about the line between its middle and outer third, and then courses outward diagonally to the axilla. From the configuration of these normal clinical margins, it will now be possible, without great difficulty, to hypothecate the necessary shift that will occur when there are pathologic changes in the lung apices. Diseases that reduce the air content will shift the medial border outward and the lateral border inward.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY†

Air Embolus Following An Attempt at Criminal Abortion

As in so many cases that the medical examiner sees, no record of the past history or physical ex-

†A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section. Letters should be addressed to Dr. Raymond S. Titus, *Secretary*, 330 Dartmouth Street, Boston.

amination was available for the following case. According to the meager history obtained, the patient was single, twenty-two years old and about eighteen weeks pregnant. She went to a female abortionist, who attempted to bring about an abortion by the use of a large bulb syringe. The patient died almost immediately. Autopsy revealed air embolus in the heart and in the lungs.

Comment. This case is reported solely because of the rarity of such a cause of death, proved by autopsy. Each year since the Maternal Mortality Study was begun, 25 to 30 fatal criminal or self-induced abortions have been reported in Massachusetts. That the above-mentioned abortion was performed in such a manner by a female abortionist probably relieves the medical profession of any responsibility. The danger of this method of abortion must be so well known to the profession that it is doubtful whether any registered physician would attempt it.

DEATH

MASON — ATHERTON P. MASON, M.D., of Fitchburg, died October 20. He was in his eighty-sixth year.

A native of Fitchburg, Dr. Mason received his degree from Harvard Medical School in 1882. He was a former president of the Worcester North District Medical Society, and was a member of the Massachusetts Medical Society and the American Medical Association.

He is survived by a daughter.

NOTICES

JEWISH MEMORIAL HOSPITAL

A diagnostic therapeutic conference will be held at the Jewish Memorial Hospital on Thursday, November 6, at 11 a.m. Dr. Valy Menkin will discuss "Inflammation."

Interested physicians and medical students are cordially invited to attend.

MASSACHUSETTS PSYCHIATRIC SOCIETY

The annual meeting of the Massachusetts Psychiatric Society, with the election of officers, will be held at the University Club, Boston, on Friday, November 7, at 6:30 p.m. The guest speaker will be Dr. Winifred Cullis, professor emeritus of physiology, University of London, whose topic will be "London Hospitals in Wartime."

NEW ENGLAND OTO-LARYNGOLOGICAL SOCIETY

The fall meeting of the New England Oto-Laryngological Society will be held at the Massachusetts Eye and Ear Infirmary, 243 Charles Street, Boston, on Wednesday, November 19, at 4:30 p.m. The clinical meeting will be followed by a buffet supper.

NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Thursday, November 6, at 7:15 p.m. in the classroom in the nurses' residence. A motion picture, "Studies in Human Fertility," will be shown. Dr. Mary I. Tompkins will be chairman.

AMERICAN ORTHOPSYCHIATRIC ASSOCIATION

The nineteenth annual meeting of the American Orthopsychiatric Association will be held at the Hotel Statler, Detroit, Michigan, on February 19, 20 and 21.

A registration fee will be charged for nonmembers. Further information may be obtained from Dr. Helen P. Langner, chairman, Publicity Committee, Vassar College, Poughkeepsie, New York.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS, UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Salem	November 3	Paul W. Hugenberger
Lowell	November 7	Albert H. Brewster
Haverhill	November 12	William T. Green
Brockton	November 13	George W. Van Gorder
Pittsfield	November 17	Frank A. Slowick
Northampton	November 19	Garry deN. Hough, Jr.
Worcester	November 21	John W. O'Meara
Fall River	November 24	Eugene A. McCarthy
Hyannis	November 25	Paul L. Norton

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, NOVEMBER 2

MONDAY, NOVEMBER 3

American College of Surgeons. Statler and Copley-Plaza hotels.
12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

TUESDAY, NOVEMBER 4

American College of Surgeons. Statler and Copley-Plaza hotels.
12:15–1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital amphitheater.

WEDNESDAY, NOVEMBER 5

American College of Surgeons. Statler and Copley-Plaza hotels.
*12:00 m. Clinicopathological conference. Children's Hospital.

THURSDAY, NOVEMBER 6

American College of Surgeons. Statler and Copley-Plaza hotels.
*8:30 a.m. Combined clinic of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital, at the Peter Bent Brigham Hospital. Conducted by Dr. Soma Weiss.
*11:00 a.m. Inflammation. Dr. Valy Menkin. Jewish Memorial Hospital.
7:15 p.m. New England Hospital for Women and Children, monthly clinical conference and meeting of staff.

FRIDAY, NOVEMBER 7

American College of Surgeons. Statler and Copley-Plaza hotels.
6:30 p.m. London Hospitals in Wartime. Dr. Winifred Cullis. Massachusetts Psychiatric Society. University Club, Boston.

*Open to the medical profession.

OCTOBER 31–JANUARY 30. Massachusetts General Hospital. Clinical staff meetings of the Children's Medical Service. Page 673, issue of October 23.
OCTOBER 31–APRIL 24. Massachusetts Memorial Hospitals. Staff meetings. Page 672, issue of October 23.
NOVEMBER 3–7. American College of Surgeons. Page vii, issue of July 31.
NOVEMBER 4. Portsmouth Naval Hospital. Page 673, issue of October 23.
NOVEMBER 5–6. American Conference on Industrial Health. Page 473, issue of September 18.
NOVEMBER 13. Pentucket Association of Physicians.
NOVEMBER 17–19, 21–22, 27 and 30. Thomas William Salmon Memorial Lectures. Page 636, issue of October 16.
NOVEMBER 19. New England Oto-Laryngological Society. Notice above.